New Year's Day.

FILE 'USPAT' ENTERED AT 09:04:30 ON 26 MAY 1998

WELCOME TO THE U. S. PATENT TEXT FILE

=> s vaccin?(P)(cell?)(P)(antigen?)(P)(express?)

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          8061 VACCIN?
        371297 CELL?
         23710 ANTIGEN?
        274708 EXPRESS?
L1 .      540 VACCIN?(P)(CELL?)(P)(ANTIGEN?)(P)(EXPRESS?)
```

=> s l1(P)(adjuvant? or cytokine?)

```
         32634 ADJUVANT?
          3301 CYTOKINE?
L2          51 L1(P)(ADJUVANT? OR CYTOKINE?)
```

=> d l2 1-51

1. 5,756,674, May 26, 1998, Peptides that induce antibodies which neutralize genetically divergent HIV-1 isolates; Hermann Katinger, et al., 530/350; 424/184.1, 188.1, 208.1; 530/329, 330 [IMAGE AVAILABLE]

2. 5,756,104, May 26, 1998, Liposome-containing intranasal vaccine formulation; Aalzen de Haan, et al., 424/206.1, 193.1, 196.11, 202.1, 212.1, 283.1, 450 [IMAGE AVAILABLE]

3. 5,747,269, May 5, 1998, Determination of peptide motifs on MHC molecules; Hans-Georg Rammensee, et al., 435/7.24, 7.5; 436/86, 89; 530/344 [IMAGE AVAILABLE]

4. 5,744,353, Apr. 28, 1998, Cytolytic T cell lines which bind to complexes of tumor rejection antigens and HLA-B44 molecules; Jean Herman, et al., 435/325, 372.3 [IMAGE AVAILABLE]

5. 5,744,347, Apr. 28, 1998, Yolk sac stem cells and their uses; Thomas E. Wagner, et al., 435/7.21 [IMAGE AVAILABLE]

6. 5,736,524, Apr. 7, 1998, Polynucleotide tuberculosis vaccine; Jean Content, et al., 514/44; 435/6, 69.1, 172.3, 320.1, 375; 935/34, 56, 62, 65 [IMAGE AVAILABLE]

7. 5,733,761, Mar. 31, 1998, Protein production and protein delivery; Douglas Treco, et al., 435/172.3, 69.4; 536/23.51, 24.1 [IMAGE AVAILABLE]

8. 5,731,168, Mar. 24, 1998, Method for making heteromultimeric polypeptides; Paul J. Carter, et al., 435/69.1, 69.7, 70.1, 71.1, 172.1, 172.3; 530/300, 350, 387.1, 387.3; 536/23.1, 23.4, 23.5, 23.53 [IMAGE AVAILABLE]

9. 5,723,127, Mar. 3, 1998, Compositions and methods for use of IL-12 as

an adjuvant; Phillip Scott, et al., 424/184.1, 191.1, 204.1, 234.1, 269.1; 530/350 [IMAGE AVAILABLE]

10. 5,714,141, Feb. 3, 1998, Use of interleukin 7 to enhance humoral immunity; Rodney Jin Yong Ho, et al., 424/85.2, 184.1, 231.1, 234.1, 450; 530/350 [IMAGE AVAILABLE]

11. 5,709,860, Jan. 20, 1998, Induction of cytotoxic T-lymphocyte responses; Syamal Raychaudhuri, et al., 424/184.1, 204.1, 208.1, 275.1, 277.1, 283.1, 400 [IMAGE AVAILABLE]

12. 5,700,649, Dec. 23, 1997, Method of detection of urinary tumor associated antigen; Donald L. Morton, et al., 435/7.1; 424/141.1, 142.1, 277.1; 435/7.9, 7.92, 7.93, 7.94; 436/507, 536 [IMAGE AVAILABLE]

13. 5,695,770, Dec. 9, 1997, Induction of cytotoxic T-lymphocyte responses; Syamal Raychaudhuri, et al., 424/278.1, 184.1, 204.1, 277.1, 283.1 [IMAGE AVAILABLE]

14. 5,693,752, Dec. 2, 1997, Peptides that induce antibodies which neutralize genetically divergent HIV-1 isolates; Hermann Katinger, et al., 530/329; 424/184.1, 188.1, 204.1, 208.1; 530/350 [IMAGE AVAILABLE]

15. 5,683,886, Nov. 4, 1997, Tumor rejection antigens which correspond to amino acid sequences in tumor rejection antigen precursor bage, and uses thereof; Pierre van der Bruggen, et al., 435/7.24; 424/93.71, 277.1; 435/7.1, 7.23; 530/324, 325, 326, 327, 328, 329, 330 [IMAGE AVAILABLE]

16. 5,679,774, Oct. 21, 1997, DNA sequences of the EBV genome, recombinant DNA molecules, processes for preparing EBV-related antigens, diagnostic compositions and pharmaceutical compositions containing said antigens; Hans J. Wolf, 530/350; 424/185.1, 196.11, 230.1; 530/300, 395; 536/23.72 [IMAGE AVAILABLE]

17. 5,660,834, Aug. 26, 1997, Monoclonal antibodies and vaccine development directed to human cancer-associated antigens by immunization with carbohydrate-carrier conjugates; Thomas J. Kjeldsen, et al., 424/277.1, 184.1, 193.1; 514/8, 23; 530/395 [IMAGE AVAILABLE]

18. 5,651,993, Jul. 29, 1997, Specific immune system modulation; Richard L. Edelson, et al., 424/534, 85.7; 514/825, 866 [IMAGE AVAILABLE]

19. 5,651,986, Jul. 29, 1997, Controlled local delivery of chemotherapeutic agents for treating solid tumors; Henry Brem, et al., 424/484, 401, 426, 486, 499 [IMAGE AVAILABLE]

20. 5,648,241, Jul. 15, 1997, Conjugate vaccine against group B streptococcus; James L. Michel, et al., 435/69.3, 252.33, 253.4, 320.1; 536/23.7 [IMAGE AVAILABLE]

21. 5,648,226, Jul. 15, 1997, Isolated peptides derived from tumor rejection antigens, and their use; Benoit Van den Eynde, et al., 435/7.24; 424/185.1, 277.1; 435/7.23; 530/326, 327, 328, 828 [IMAGE AVAILABLE]

22. 5,637,483, Jun. 10, 1997, Irradiated tumor cell vaccine engineered to express GM-CSF; Glenn Dranoff, et al., 424/93.21; 435/320.1; 514/44; 935/57, 62, 71 [IMAGE AVAILABLE]

23. 5,635,188, Jun. 3, 1997, Anti-cancer vaccine; Jean-Claude Bystryn, 424/277.1; 514/2, 8, 12; 530/350, 395 [IMAGE AVAILABLE]

24. 5,627,048, May 6, 1997, Aedes aegypti densovirus expression system; Boris N. Afanasiev, et al., 435/69.1, 320.1, 348 [IMAGE AVAILABLE]

25. 5,626,862, May 6, 1997, Controlled local delivery of chemotherapeutic agents for treating solid tumors; Henry Brem, et al., 424/426, 1.11, 425 [IMAGE AVAILABLE]

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28. 5,612,201, Mar. 18, 1997, Isolated nucleic acid molecules useful in determining expression of a tumor rejection antigen precursor; Etienne De Plaen, et al., 435/91.2, 6; 536/23.1, 24.33 [IMAGE AVAILABLE]

29. 5,610,013, Mar. 11, 1997, Method for diagnosing a disorder by determining expression of gage tumor rejection antigen precursors; Benoit Van den Eynde, et al., 435/6, 7.1, 252.3, 252.33, 320.1, 325, 358, 362, 365; 536/23.5 [IMAGE AVAILABLE]

30. 5,591,632, Jan. 7, 1997, Recombinant BCG; Michael A. O'Donnell, et al., 435/252.3, 253.1, 320.1 [IMAGE AVAILABLE]

31. 5,589,334, Dec. 31, 1996, Isolated nucleic acid molecule which codes for a tumor rejection antigen precursor which is processed to an antigen presented by HLA-B44, and uses thereof; Pierre Coulie, et al., 435/6, 252.3, 252.33, 320.1; 536/23.1, 24.33 [IMAGE AVAILABLE]

32. 5,585,103, Dec. 17, 1996, Induction of cytotoxic T-lymphocyte responses; Syamal Raychaudhuri, et al., 424/278.1, 204.1, 277.1, 283.1, 420 [IMAGE AVAILABLE]

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34. 5,571,515, Nov. 5, 1996, Compositions and methods for use of IL-12 as an adjuvant; Phillip Scott, et al., 424/208.1, 204.1, 234.1; 530/350 [IMAGE AVAILABLE]

35. 5,549,898, Aug. 27, 1996, Immunogenic anaplasma marginale surface antigens, compositions, and methods of use; Travis C. McGuire, et al., 424/269.1, 265.1, 266.1, 270.1 [IMAGE AVAILABLE]

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37. 5,504,005, Apr. 2, 1996, Recombinant mycobacterial vaccine; Barry R. Bloom, et al., 435/253.1, 69.1, 69.3, 69.51, 69.52, 172.1, 172.3, 183, 189, 207, 252.33, 320.1 [IMAGE AVAILABLE]

38. 5,457,035, Oct. 10, 1995, Cytokine which is a ligand for OX40; Peter R. Baum, et al., 435/69.5, 252.3, 320.1, 364; 530/351; 536/23.5; 935/9 [IMAGE AVAILABLE]

39. 5,334,379, Aug. 2, 1994, Cytokine and hormone carriers for conjugate vaccines; Subramonia Pillai, et al., 424/85.2, 85.1, 85.4, 197.11, 244.1, 250.1, 831; 530/351, 395, 404, 405, 406, 411 [IMAGE AVAILABLE]

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against feline immunodeficiency virus; Janet K. Yamamoto, et al., 424/208.1, 819 [IMAGE AVAILABLE]

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43. 5,247,069, Sep. 21, 1993, Ligands and methods for augmenting B-cell proliferation; Jeffrey A. Ledbetter, et al., 530/350, 380, 395, 829 [IMAGE AVAILABLE]

44. 5,198,535, Mar. 30, 1993, Protective malaria sporozoite surface protein immunogen and gene; Stephen L. Hoffman, et al., 530/350, 300 [IMAGE AVAILABLE]

45. 5,182,368, Jan. 26, 1993, Ligands and methods for augmenting B-cell proliferation; Jeffrey A. Ledbetter, et al., 530/388.73; 435/188; 530/350, 351, 391.3, 391.7, 866 [IMAGE AVAILABLE]

46. 5,149,529, Sep. 22, 1992, Compositions and treatment for herpes simplex; Rodney Ho, et al., 424/196.11, 85.5, 231.1, 279.1, 283.1, 452, 812; 514/8 [IMAGE AVAILABLE]

47. 5,112,749, May 12, 1992, Vaccines for the malaria circumsporozoite protein; Robert N. Brey, III, et al., 435/172.3, 69.1, 252.3, 320.1, 879; 530/350; 536/23.4, 23.7, 24.1; 935/12, 27, 41, 56, 65, 72 [IMAGE AVAILABLE]

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50. 4,357,421, Nov. 2, 1982, Synthetic gene coding for influenza hemagglutinin; John S. Emtage, et al., 435/68.1, 69.8, 91.51, 172.3, 252.33, 320.1; 530/350, 358; 536/23.7, 23.72, 24.1; 930/220; 935/11, 18, 20, 41, 65 [IMAGE AVAILABLE]

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=> d l2 45 kwic

US PAT NO: 5,182,368 [IMAGE AVAILABLE] L2: 45 of 51

DETDESC:

DETD(51)

The . . . in their unmodified or modified forms to modulate immune responses. For example, the ligands themselves may be used as an "**adjuvant**" to increase an immune response to a **vaccine** or to increase the immune response of an immunosuppressed individual. Alternatively, if cytotoxins or anti-proliferative agents are coupled to the. . . or in transplant patients to obviate graft rejection. These modified ligands could also be used to treat malignancies that comprise

cells or tumors which **express** the Bp50 **antigen** whether or not the malignancy is B-**cell** in origin.

=> d l2 7,9,10,17,23,25,34,38,39 date

L2: 7 of 51

TITLE: Protein production and protein delivery
US PAT NO: 5,733,761 DATE ISSUED: Mar. 31, 1998
[IMAGE AVAILABLE]
APPL-NO: 08/451,893 DATE FILED: May 26, 1995
REL-US-DATA: Continuation of Ser. No. 985,586, Dec. 3, 1992, abandoned, which is a continuation-in-part of Ser. No. 789,188, Nov. 5, 1991, abandoned, Ser. No. 911,533, Jul. 10, 1992, abandoned, and Ser. No. 787,840, Nov. 5, 1991, abandoned.

L2: 9 of 51

TITLE: Compositions and methods for use of IL-12 as an adjuvant
US PAT NO: 5,723,127 DATE ISSUED: Mar. 3, 1998
[IMAGE AVAILABLE]
APPL-NO: 08/621,493 DATE FILED: Mar. 25, 1996
REL-US-DATA: Division of Ser. No. 265,087, Jun. 17, 1994, Pat. No. 5,571,515, which is a continuation-in-part of Ser. No. 229,282, Apr. 18, 1994, abandoned.

L2: 10 of 51

TITLE: Use of interleukin 7 to enhance humoral immunity
US PAT NO: 5,714,141 DATE ISSUED: Feb. 3, 1998
[IMAGE AVAILABLE]
APPL-NO: 08/458,032 DATE FILED: Jun. 1, 1995
REL-US-DATA: Continuation of Ser. No. 41,672, Apr. 1, 1993, abandoned.

L2: 17 of 51

TITLE: Monoclonal antibodies and vaccine development directed to human cancer-associated antigens by immunization with carbohydrate-carrier conjugates
US PAT NO: 5,660,834 DATE ISSUED: Aug. 26, 1997
[IMAGE AVAILABLE]
APPL-NO: 08/400,480 DATE FILED: Mar. 8, 1995
REL-US-DATA: Continuation of Ser. No. 705,431, May 24, 1991, abandoned, which is a continuation-in-part of Ser. No. 317,492, Mar. 1, 1989, abandoned, which is a continuation-in-part of Ser. No. 167,786, Mar. 11, 1988, abandoned.

L2: 23 of 51

TITLE: Anti-cancer vaccine
US PAT NO: 5,635,188 DATE ISSUED: Jun. 3, 1997
[IMAGE AVAILABLE]
APPL-NO: 08/367,682 DATE FILED: Dec. 30, 1994
REL-US-DATA: Continuation of Ser. No. 210,243, Mar. 18, 1994, abandoned, which is a continuation of Ser. No. 717,972, Jun. 20, 1991, abandoned, which is a continuation of Ser. No. 485,780, Feb. 22, 1990, Pat. No. 5,030,621, which is a continuation of Ser. No. 41,864, Apr. 23, 1987, abandoned.

L2: 25 of 51

TITLE: Controlled local delivery of chemotherapeutic agents for treating solid tumors
US PAT NO: 5,626,862 DATE ISSUED: May 6, 1997
[IMAGE AVAILABLE]
APPL-NO: 08/284,341 DATE FILED: Aug. 2, 1994

L2: 34 of 51

TITLE: Compositions and methods for use of IL-12 as an adjuvant
US PAT NO: 5,571,515 DATE ISSUED: Nov. 5, 1996
[IMAGE AVAILABLE]
APPL-NO: 08/265,087 DATE FILED: Jun. 17, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 229,282, Apr. 18, 1994, abandoned.

L2: 38 of 51

TITLE: Cytokine which is a ligand for OX40
US PAT NO: 5,457,035 DATE ISSUED: Oct. 10, 1995
[IMAGE AVAILABLE]
APPL-NO: 08/097,827 DATE FILED: Jul. 23, 1993

L2: 39 of 51

TITLE: Cytokine and hormone carriers for conjugate vaccines
US PAT NO: 5,334,379 DATE ISSUED: Aug. 2, 1994
[IMAGE AVAILABLE]
APPL-NO: 07/553,901 DATE FILED: Jul. 16, 1990
REL-US-DATA: Continuation-in-part of Ser. No. 380,566, Jul. 14, 1989.

=> d l2 7,9,10,17,23,25,34,38,39 kwic

US PAT NO: 5,733,761 [IMAGE AVAILABLE] L2: 7 of 51

DETDESC:

DETD(2)

The present invention and the methods described in the applications incorporated herein by reference relate to transfected primary, secondary, and immortalized **cells** of vertebrate origin, particularly mammalian origin, transfected with exogenous genetic material (DNA or RNA) which encodes a clinically useful product, methods by which primary, secondary, and immortalized **cells** are transfected to include exogenous genetic material, methods of producing clonal **cell** strains or heterogenous **cell** strains which **express** exogenous genetic material, a method of providing clinically useful products in physiologically useful quantities to an individual in need thereof through the use of transfected **cells** of the present invention, methods of **vaccinating** animals for protection against pathogenic viruses or microbial agents **expressing** epitopes **antigenically** related to products **expressed** by the transfected **cells** and methods of producing antibodies directed against a product made by the transfected primary, secondary, or immortalized **cells**. Clinically useful products can be produced in vitro, by purification from the transfected **cells**, or produced in vivo, by implantation into a non-human animal or human (i.e., gene therapy). Whether produced in vitro or in vivo, the clinically useful products can include hormones, **cytokines**, **antigens**, antibodies, enzymes, clotting factors, transport proteins, receptors, regulatory proteins, structural proteins, transcription factors, anti-sense RNA. Additionally, the methods of the present invention can be used to produce **cells** which produce non-naturally occurring ribozymes, proteins, or nucleic acids.

US PAT NO: 5,723,127 [IMAGE AVAILABLE] L2: 9 of 51

SUMMARY:

BSUM(18)

In . . . the invention provides a therapeutic composition for the treatment or amelioration of the symptoms of cancer, and a method for **adjuvanting** a therapeutic cancer "**vaccine**". A cancer **vaccine** or therapeutic may comprise an **antigen expressed** on the surface

of a cancer **cell**. This **antigen** may be naturally present on the cancer **cell**. Alternatively, the cancer **cell** may be manipulated ex vivo and transfected with a selected **antigen**, which it then **expresses** when introduced into the patient. An exemplary therapeutic composition described herein can contain the protein B7 (either alone as a protein, biologically active fragment or `naked` DNA encoding same) or preferably a B7 transfected cancer **cell** in combination with IL-12 (as protein and/or subunit, `naked` DNA or transduced DNA or a biologically active fragment thereof). The co-administration of IL-12 with a B7 preparation enhances the T-**cell** stimulating activity of the B7 preparation.

DETDESC:

DETD(3)

The present invention also provides novel therapeutic compositions and methods of **adjuvantation** intended to provide a synergistic effect with certain therapeutic compositions, particularly so-called "cancer **vaccines**", which include a selected **antigen** occurring naturally on a cancer **cell** or a cancer **cell** transfected with, and capable of **expressing**, a selected **antigen**, e.g., B7. Such compositions may demonstrate an enhanced proliferative effect on T **cells** and **cytokine** production thereby. This proliferative effect may exhibit some resistance to chemotherapeutics and thus provide another therapeutic agent and regimen for. . .

DETDESC:

DETD(13)

In addition to the administration of the IL-12 protein as an **adjuvant**, it is also anticipated that nucleic acid sequences encoding IL-12 or a fragment thereof may be used as an **adjuvant**. The nucleic acid sequences, preferably in the form of DNA, may be delivered to a **vaccinate** for in vivo **expression** of the IL-12 protein or peptide. So-called `naked DNA` may be used to **express** the IL-12 protein or peptide fragment in vivo in a patient. [See, e.g., J. Cohen, Science, 259:1691-1692 (Mar. 19, 1993);. . . may be incorporated, or transduced, into the microorganism itself, if the whole pathogen itself is to be employed as the **vaccinal antigen**. Alternatively, IL-12 DNA may be administered as part of the **vaccine** composition or separately, but contemporaneously with the **vaccine antigen**, e.g., by injection. Still other modes of delivering IL-12 to the **vaccinate** in the form of DNA are known to those of skill in the art and may be employed rather than. . . into a nucleic acid cassette. This cassette may be engineered to contain, in addition to the IL-12 sequence to be **expressed**, other optional flanking sequences which enable its insertion into a vector. This cassette may then be inserted into an appropriate. . . of a promoter, an mRNA leader sequence, an initiation site and other regulatory sequences capable of directing the replication and **expression** of that sequence in vivo. This vector permits infection of **vaccinate**'s **cells** and **expression** of the IL-12 in vivo.

DETDESC:

DETD(14)

When IL-12 nucleic acid sequences are used as an **adjuvant**, these sequences may be operably linked to DNA sequences which encode the **antigen**. Hence, the vector or cassette, as described above, encoding the IL-12 DNA sequences may additionally include sequences encoding the **antigen**. Each of these sequences may be operatively linked to the promoter sequence of the vector or cassette. Alternatively, `naked DNA`

encoding the **antigen**-may be in a separate plasmid. Where present in one or two plasmids, the naked DNA encoding the **antigen** and/or IL-12, upon introduction into the host **cells**, permits the infection of **vaccinate**'s **cells** and **expression** of both IL-12 and the **antigen** in vivo.

DETDESC:

DETD(20)

It is further anticipated that IL-12 can be used as an **adjuvant** in so-called therapeutic **vaccines** for certain cancers and solid tumors, in a manner similar to that disclosed above for its use as an **adjuvant** for **vaccines** containing **antigens** of a pathogenic microorganism. Particularly where CMI is considered a component of protection against the particular cancer, the use of IL12 as an **adjuvant** in a cancer **vaccine** or therapeutic is encompassed by the present invention. Cancer **vaccines** typically include an **antigen** **expressed** on and isolated from a cancer **cell** or a cancer **cell** transfected with, and capable of **expressing**, a selected **antigen**. For example, any purified tumor **antigen** may be co-administered with IL-12 as described above for pathogenic **vaccines**. identification of relevant cancer **antigens** will permit the development of such **vaccines**. Alternatively, other cancer therapeutics are designed using an **antigen** normally not **expressed** on a cancer **cell**. That selected **antigen** is transfected into the cancer **cell** and the transfected **cell** itself, **expressing** the **antigen**, is used as the **vaccine** or therapeutic. Such a **vaccine** or therapeutic may be co-administered with IL-12 to obtain the **adjuvantation** effect. The **adjuvantation** of such **vaccines** can be accomplished by resort to the above disclosure by one of skill in the art.

US PAT NO: 5,714,141 [IMAGE AVAILABLE] L2: 10 of 51

DETDESC:

DETD(59)

The results showed that liposome-formulated **antigen** **vaccine** induced higher antibody titer than alum-associated **antigen** **vaccine**, and these antibody responses can be enhanced by administration of IL-7 liposomes. Spleen **cells** were harvested on days 21, 35 and 42 to evaluate cytotoxic T lymphocyte (CTL) response directed against autologous **cells** infected with **vaccinia** virus **expressing** HIV-env protein. Mice treated with liposome-formulated **antigen** **expressed** the highest CTL activity, regardless of whether IL-7 liposome was given as an immune potentiator (**adjuvant**) (FIG. 4). In contrast, spleen **cells** from mice **vaccinated** with alum-associated **antigen** exhibited minimal CTL response, which can be enhanced by concurrent (simultaneous) IL-7 liposome treatment (FIG. 1). Collectively, IL-7 liposome treatment. . . the alum-associated or liposome-formulated env-2-3 (Tables 1 and 2) while its enhancement on CTL activity was only detected with mice **vaccinated** with alum-associated **antigen** (FIG. 1).

US PAT NO: 5,660,834 [IMAGE AVAILABLE] L2: 17 of 51

ABSTRACT:
A **vaccine** and method to prevent growth and replication of cancer **cells** that **express** a core structure of a mucin-type glycoprotein is disclosed. The **vaccine** comprises: (a) a pharmaceutically effective amount of an **antigen** comprising a purified mucin-type glycoprotein or a chemically synthesized mucin-type glycoprotein carbohydrate determinant conjugated to a carrier peptide or macromolecule, wherein said mucin-type glycoprotein **expresses** or carries the core structure of a mucin-type

glycoprotein **expressed** on said cancer **cells**; and (b) a pharmaceutically acceptable carrier including natural or synthetic **adjuvants**. The method comprises administering the above-described **vaccine** to a host. A medicament and method for treating cancer wherein the cancer **cells express** a core structure of a mucin-type glycoprotein is disclosed. The medicament comprises: (a) a pharmaceutically effective amount of an anti-cancer. . .

US PAT NO: 5,635,188 [IMAGE AVAILABLE] L2: 23 of 51

ABSTRACT:
A human anti-cancer **vaccine** is prepared by culturing human cancer **cells**, such as human melanoma **cells**, in a serum-free medium. The cancer **cells** are selected on the basis of **expressing** different patterns of **cell** surface tumor **antigens** and are adapted and grown in a serum-free medium. During culturing, **cell** surface **antigens** of the cancer **cells** are shed into the culture medium. The culture medium, after removal of the cancer **cells**, containing the shed cancer **cell antigens** is concentrated. When used as an anti-cancer **vaccine**, the resulting concentrated composition is administered to the patient, such as intradermally. In the instance where patients are cancer patients, the **vaccine** is administered to the patient intradermally over a period of weeks with or without an **adjuvant**.

US PAT NO: 5,626,862 [IMAGE AVAILABLE] L2: 25 of 51

DETDESC:

DETD(22)

Therapeutic . . . and enhancement of a local inflammatory response to the tumor. Granulocyte-macrophage colony stimulating factor (GM-CSF) is an example of a **cytokine** systemically activating cytotoxic T lymphocytes (CTL) which has been shown to lead to the elimination of tumor **cells** in a potent and specific manner, by stimulating the growth and activity of several myeloid **cells** and playing a critical role in the migration and development of professional **antigen** present **cells** such as dendritic **cells**. Tumor specific CTL induction and systemic protection from tumor challenge can be generated by the subcutaneous injection of irradiated tumor **cells** genetically modified to produce the **cytokine** granulocyte-macrophage colony stimulating factor (GM-CSF). In one embodiment, killed tumor **cells** are transduced with the gene encoding GM-CSF and administered as a **vaccine** to stimulate CTL activation. This can be done prior to or in combination with implantation or local delivery of the chemotherapeutic agents. Other **cytokines** such as interleukin 2 (IL-2), tumor necrosis factor (TNF) and IL-4, as well as IL-5, IL-6 and gamma interferon (although. . . stimulate tumor responses. IL-2 induces a local inflammatory response leading to activation of both helper and cytotoxic subsets of T **cells**. IL-4 has broad immunoregulatory properties. TNF-.alpha. has a diverse range of biological properties including generation of a number of **cytokines** such as IL-6, IL8, GM-CSF, and G-CSF, as well as the generation of hemorrhagic necrosis in established tumors. These are highly effective if administered in the polymeric matrix with the chemotherapeutic drug or in the form of transduced **cells** **expressing** IL-2 which are co-administered to the animal. Other **vaccines** and immunotoxins are also well known to those skilled in the art.

US PAT NO: 5,571,515 [IMAGE AVAILABLE] L2: 34 of 51

SUMMARY:

BSUM(18)

In . . . the invention provides a therapeutic composition for the treatment or amelioration of the symptoms of cancer, and a method for **adjuvanting** a therapeutic cancer "**vaccine**". A cancer **vaccine** or therapeutic may comprise an **antigen expressed** on the surface of a cancer **cell**. This **antigen** may be naturally present on the cancer **cell**. Alternatively, the cancer **cell** may be manipulated ex vivo and transfected with a selected **antigen**, which it then **expresses** when introduced into the patient. An exemplary therapeutic composition described herein can contain the protein B7 (either alone as a protein, biologically active fragment or `naked` DNA encoding same) or preferably a B7 transfected cancer **cell** in combination with IL-12 (as protein and/or subunit, `naked` DNA or transduced DNA or a biologically active fragment thereof). The co-administration of IL-12 with a B7 preparation enhances the T-**cell** stimulating activity of the B7 preparation.

DETDESC:

DETD(3)

The present invention also provides novel therapeutic compositions and methods of **adjuvantation** intended to provide a synergistic effect with certain therapeutic compositions, particularly so-called "cancer **vaccines**", which include a selected **antigen** occurring naturally on a cancer **cell** or a cancer **cell** transfected with, and capable of **expressing**, a selected **antigen**, e.g., B7. Such compositions may demonstrate an enhanced proliferative effect on T **cells** and **cytokine** production thereby. This proliferative effect may exhibit some resistance to chemotherapeutics and thus provide another therapeutic agent and regimen for. . .

DETDESC:

DETD(13)

In addition to the administration of the IL-12 protein as an **adjuvant**, it is also anticipated that nucleic acid sequences encoding IL-12 or a fragment thereof may be used as an **adjuvant**. The nucleic acid sequences, preferably in the form of DNA, may be delivered to a **vaccinate** for in vivo **expression** of the IL-12 protein or peptide. So-called `naked DNA` may be used to **express** the IL-12 protein or peptide fragment in vivo in a patient. [See, e.g., J. Cohen, Science, 259:1691-1692 (Mar. 19, 1993);. . . may be incorporated, or transduced, into the microorganism itself, if the whole pathogen itself is to be employed as the **vaccinal antigen**. Alternatively, IL-12 DNA may be administered as part of the **vaccine** composition or separately, but contemporaneously with the **vaccine antigen**, e.g., by injection. Still other modes of delivering IL-12 to the **vaccinate** in the form of DNA are known to those of skill in the art and may be employed rather than. . . into a nucleic acid cassette. This cassette may be engineered to contain, in addition to the IL-12 sequence to be **expressed**, other optional flanking sequences which enable its insertion into a vector. This cassette may then be inserted into an appropriate. . . of a promoter, an mRNA leader sequence, an initiation site and other regulatory sequences capable of directing the replication and **expression** of that sequence in vivo. This vector permits infection of **vaccinate**'s **cells** and **expression** of the IL-12 in vivo.

DETDESC:

DETD(14)

When IL-12 nucleic acid sequences are used as an **adjuvant**, these sequences may be operably linked to DNA sequences which encode the

antigen. Hence, the vector or cassette, as described above, encoding the IL-12 DNA sequences may additionally include sequences encoding the **antigen**. Each of these sequences may be operatively linked to the promoter sequence of the vector or cassette. Alternatively, `naked DNA` encoding the **antigen** may be in a separate plasmid. Where present in one or two plasmids, the naked DNA encoding the **antigen** and/or IL-12, upon introduction into the host **cells**, permits the infection of **vaccinate**'s **cells** and **expression** of both IL-12 and the **antigen** in vivo.

DETDESC:

DETD(20)

It is further anticipated that IL-12 can be used as an **adjuvant** in so-called therapeutic **vaccines** for certain cancers and solid tumors, in a manner similar to that disclosed above for its use as an **adjuvant** for **vaccines** containing **antigens** of a pathogenic microorganism. Particularly where CMI is considered a component of protection against the particular cancer, the use of IL-12 as an **adjuvant** in a cancer **vaccine** or therapeutic is encompassed by the present invention. Cancer **vaccines** typically include an **antigen** **expressed** on and isolated from a cancer **cell** or a cancer **cell** transfected with, and capable of **expressing**, a selected **antigen**. For example, any purified tumor **antigen** may be co-administered with IL-12 as described above for pathogenic **vaccines**. Identification of relevant cancer **antigens** will permit the development of such **vaccines**. Alternatively, other cancer therapeutics are designed using an **antigen** normally not **expressed** on a cancer **cell**. That selected **antigen** is transfected into the cancer **cell** and the transfected **cell** itself, **expressing** the **antigen**, is used as the **vaccine** or therapeutic. Such a **vaccine** or therapeutic may be co-administered with IL-12 to obtain the **adjuvantation** effect. The **adjuvantation** of such **vaccines** can be accomplished by resort to the above disclosure by one of skill in the art.

US PAT NO: 5,457,035 [IMAGE AVAILABLE] L2: 38 of 51

DETDESC:

DETD(26)

The ability of OX40-L to co-stimulate T **cell** proliferation and **cytokine** secretion suggests a role for OX40-L as an autocrine growth ligand in T **cell** activation. Furthermore, native OX40-L is a plasma membrane protein, and may be involved in direct **cell**-dependent interactions between T **cells**. Thus, the OX40/OX40-L interaction may comprise a component of the adhesion of T **cells** to one another that is seen following activation with **antigen** or mitogen. Moreover, the stimulation of IL-2 and IL-4 secretion suggests that OX40-L has its effect upon the TH0 and/or TH2 subpopulations of T **cells** (Mosmann and Coffman, Immunol, Today 8:223, 1987; Mosmann and Coffman, Adv. Immunol. 46:111, 1988). It is known in the art that generation of TH2 versus TH1 populations of T **cells** will have an effect upon the type and effectiveness of the ensuing immune response (Coffman et al., Immuno. Rev. 123:189;. . . modify a number of immune responses, including the nature of the immunoglobulin isotype generated and the development of cytolytic T **cells**. Therefore, OX40-L is likely to be useful in inducing a TH2 immune response, for example as a **vaccine** **adjuvant**, or in ex vivo techniques to stimulate selected populations of TH2 **cells**. An OX40-L antagonist may similarly be useful in directing an immune response toward a TH1 response or in inhibiting TH2 responses. OX40-L will also be useful as an in vitro reagent for the culture of primary T **cells** and the development of clonal T **cells** lines, or for the detection of **cells** **expression** OX40 or an OX40

homolog.

US PAT NO: 5,334,379 [IMAGE AVAILABLE] L2: 39 of 51

SUMMARY:

BSUM(8)

This invention pertains to immunogenic conjugates and **vaccine** compositions containing the immunogenic conjugate. The conjugates comprise an **antigen** (not normally associated with the **cytokine**, lymphokine, hormone or growth factor), especially a carbohydrate containing **antigen**, bound to a **cytokine**, lymphokine, hormone or growth factor having immunomodulating activity, wherein the **cytokine**, lymphokine, hormone or growth factor modifies the immunogenic activity of the **antigen**. The **cytokine** or lymphokine can be an interleukin, such as interleukin-1.alpha., interleukin-1.beta., interleukin-2, an interferon, such as interferon gamma, or other **cytokine** or lymphokine which has immunomodulating activity. The hormone or growth factor can be of bovine, porcine or chicken origin, for. . . stimulating factor (GCSF), insulin-like growth factor (IGF-1), somatotropin or insulin, or any other hormone or growth factor whose receptor is **expressed** on **cells** of the immune system.

```
  s (cd40L or cd40(w)ligand or gp39 or 5c8) and (vaccin? or adjuvant?)

            1515  CD40L
            5612  CD40
          192014  LIGAND
            2178  CD40(W)LIGAND
             392  GP39
              64  5C8
          195416  VACCIN?
           86286  ADJUVANT?
      S3      81  (CD40L OR CD40(W)LIGAND OR GP39 OR 5C8) AND (VACCIN? OR
                  ADJUVANT?)
? rd s3

>>>Duplicate detection is not supported for File 351.

>>>Records from unsupported files will be retained in the RD set.
...examined 50 records  (50)
...completed examining records
      S4      50  RD S3 (unique items)
? t s4/3/all


 4/3/1     (Item 1 from file: 55)
DIALOG(R)File  55:BIOSIS PREVIEWS(R)
(c) 1998 BIOSIS. All rts. reserv.

14184590     BIOSIS Number: 01184590
  The induction of a protective response in Leishmania major-infected
BALB-c mice with anti-CD40 mAb
  Ferlin W G; Von Der Weid T; Cottrez F; Ferrick D A; Coffman R L; Howard M
C
  Anergen Inc., 301 Penobscot Dr., Redwood City, CA 94036, USA
  European Journal of Immunology 28 (2). 1998.  525-531.
  Full Journal Title:  European Journal of Immunology
  ISSN: 0014-2980
  Language: ENGLISH
  Print Number: Biological Abstracts Vol. 105 Iss. 009 Ref. 127302


 4/3/2     (Item 2 from file: 55)
DIALOG(R)File  55:BIOSIS PREVIEWS(R)
(c) 1998 BIOSIS. All rts. reserv.

14153776     BIOSIS Number: 01153776
  Upregulation of CD40 ligand and IL-4 expression by the
23-valent pneumococcal vaccine in children with recurrent infections
  Ortigas A P; Butler B; Leiva L E; Sorensen R U
  LSU Med. Cent., New Orleans, LA, USA
  Journal of Allergy and Clinical Immunology 101 (1 PART 2). 1998.  S15.
  Full Journal Title:  54th Annual Meeting of the American Academy of
Allergy, Asthma and Immunology, Washington, DC, USA, March 13-18, 1998.
Journal of Allergy and Clinical Immunology
  ISSN: 0091-6749
  Language: ENGLISH
  Document Type: CONFERENCE PAPER
  Print Number: Biological Abstracts/RRM Vol. 050 Iss. 004 Ref. 061660
```

4/3/3 (Item 3 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

14153358 BIOSIS Number: 01153358
Upregulation of **CD40L** and the Th2 response induced by immunization with the 23-valent pneumococcal **vaccine**
Butler B; Leiva L E; Sorensen R U
Dep. Pediatrics, La. State Univ. Med. Center, New Orleans, LA, USA
Journal of Investigative Medicine 46 (1). 1998. 28A.
Full Journal Title: Meeting of the Southern Section of the American Federation for Medical Research, New Orleans, Louisiana, USA, February 7-9, 1998. Journal of Investigative Medicine
ISSN: 1081-5589
Language: ENGLISH
Document Type: CONFERENCE PAPER
Print Number: Biological Abstracts/RRM Vol. 050 Iss. 004 Ref. 061242

4/3/4 (Item 4 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

13814780 BIOSIS Number: 99814780
A Leishmania protein that modulates interleukin (IL)-12, IL-10 and tumor necrosis factor-alpha production and expression of B7-1 in human monocyte-derived antigen-presenting cells
Probst P; Skeiky Y A W; Steeves M; Gervassi A; Grabstein K H; Reed S G
1124 Columbia, Suite 464, Seattle, WA 98104, USA
European Journal of Immunology 27 (10). 1997. 2634-2642.
Full Journal Title: European Journal of Immunology
ISSN: 0014-2980
Language: ENGLISH
Print Number: Biological Abstracts Vol. 104 Iss. 012 Ref. 172384

4/3/5 (Item 5 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

13803066 BIOSIS Number: 99803066
Efficient adenovirus-mediated gene transduction of normal and leukemic hematopoietic cells
Huang M R; Olsson M; Kallin A; Pettersson U; Totterman T H
Dep. Clinical Immunology, Univ. Hospital, S-751 85 Uppsala, Sweden
Gene Therapy 4 (10). 1997. 1093-1099.
Full Journal Title: Gene Therapy
ISSN: 0969-7128
Language: ENGLISH
Print Number: Biological Abstracts Vol. 104 Iss. 011 Ref. 160670

4/3/6 (Item 6 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

13763548 BIOSIS Number: 99763548
Recombinant viruses as **vaccines** and immunological tools
Rolph M S; Ramshaw I A
Dep. Immunol., Max Planck Inst. Infection Biol., Monbijoustrasse 2, D-10117 Berlin, Germany
Current Opinion in Immunology 9 (4). 1997. 517-524.
Full Journal Title: Current Opinion in Immunology
ISSN: 0952-7915
Language: ENGLISH

Print Number: Biological Abstracts/RRM Vol. 049 Iss. 011 Ref. 185266

4/3/7 (Item 7 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

13659284 BIOSIS Number: 99659284
Normal B cells fail to secrete interleukin-12
Guery J-C; Ria F; Galbiati F; Adorini L
Roche Milano Richerche, Via Olgettina 58, I-20132 Milano, Italy
European Journal of Immunology 27 (7). 1997. 1632-1639.
Full Journal Title: European Journal of Immunology
ISSN: 0014-2980
Language: ENGLISH
Print Number: Biological Abstracts Vol. 104 Iss. 005 Ref. 067683

4/3/8 (Item 8 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

13646832 BIOSIS Number: 99646832
Protective immunity induced by tumor **vaccines** requires interaction between CD40 and its ligand, CD154
Mackey M F; Gunn J R; Ting P P; Kikutani H; Dranoff G; Noelle R J; Barth R J Jr
Sect. Gen. Surg., Dartmouth-Hitchcock Medical Cent., One Medical Center Drive, Lebanon, NH 03756, USA
Cancer Research 57 (13). 1997. 2569-2574.
Full Journal Title: Cancer Research
ISSN: 0008-5472
Language: ENGLISH
Print Number: Biological Abstracts Vol. 104 Iss. 004 Ref. 055231

4/3/9 (Item 9 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

13529651 BIOSIS Number: 99529651
CD40-**CD40L** interactions have a critical role in T cell priming induced by tumor **vaccines**
Barth R; Mackey M; Gunn J; Ting P; Noelle R
Dep. Surgery, Dartmouth Med. Sch., Norris Cotton Cancer Cent., Lebanon, NH 03756, USA
Proceedings of the American Association for Cancer Research Annual Meeting 38 (0). 1997. 37.
Full Journal Title: Eighty-eighth Annual Meeting of the American Association for Cancer Research, San Diego, California, USA, April 12-16, 1997. Proceedings of the American Association for Cancer Research Annual Meeting
ISSN: 0197-016X
Language: ENGLISH
Document Type: CONFERENCE PAPER
Print Number: Biological Abstracts/RRM Vol. 049 Iss. 006 Ref. 094431

4/3/10 (Item 10 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

13472737 BIOSIS Number: 99472737
Suppression of murine thyroiditis via blockade of the CD40-**CD40L** interaction

Carayanniotis G; Masters S R; Noelle R J
Fac. Med., Health Sci. Cent., 300 Prince Philip Dr., St. John's, Newfoundland A1B 3V6, Canada
Immunology 90 (3). 1997. 421-426.
Full Journal Title: Immunology
ISSN: 0019-2805
Language: ENGLISH
Print Number: Biological Abstracts Vol. 103 Iss. 009 Ref. 128406

4/3/11 (Item 11 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

13185651 BIOSIS Number: 99185651
Development of immune functions related to allergic mechanisms in young children
Koning H; Baert M R M; Oranje A P; Savelkoul H F J; Neijens H J
Dep. Immunol., Erasmus Univ., Dr. Molewaterplein 50, 3015 GE Rotterdam, Netherlands
Pediatric Research 40 (3). 1996. 363-375.
Full Journal Title: Pediatric Research
ISSN: 0031-3998
Language: ENGLISH
Print Number: Biological Abstracts Vol. 102 Iss. 008 Ref. 117658

4/3/12 (Item 12 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

13185422 BIOSIS Number: 99185422
Differential activation requirements of isotype-switched B cells
Ehrhardt R O; Harriman G R; Inman J K; Lycke N; Gray B; Strober W
Mucosal Immunity Sect., LCI, NIAID, Natl. Inst. Health, Bethesda, MD 20892, USA
European Journal of Immunology 26 (8). 1996. 1926-1934.
Full Journal Title: European Journal of Immunology
ISSN: 0014-2980
Language: ENGLISH
Print Number: Biological Abstracts Vol. 102 Iss. 008 Ref. 117429

4/3/13 (Item 13 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

13039447 BIOSIS Number: 99039447
CD40-**CD40 ligand** interactions are critical in T-B cooperation but not for other anti-viral VD4+ T cell functions
Oxenius A; Campbell K A; Maliszewski C R; Kishimoto T; Kikutani H; Hengartner H; Zinkernagel R M; Bachmann M F
Inst. Exp. Immunol., Schmelzbergstr. 12, CH-8091 Zurich, Switzerland
Journal of Experimental Medicine 183 (5). 1996. 2209-2218.
Full Journal Title: Journal of Experimental Medicine
ISSN: 0022-1007
Language: ENGLISH
Print Number: Biological Abstracts Vol. 102 Iss. 002 Ref. 021620

4/3/14 (Item 14 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11714653 BIOSIS Number: 98314653

CD40 ligand has potent antiviral activity
Ruby J; Bluethmann H; Aguet M; Ramshaw I A
Viral Eng. Cytokines Group, Div. Cell Biol., John Curtin Sch. Med. Res., P.O. Box 334, Canberra 2601, Australia
Nature Medicine 1 (5). 1995. 437-441.
Full Journal Title: Nature Medicine
ISSN: 1078-8956
Language: ENGLISH
Print Number: Biological Abstracts Vol. 100 Iss. 002 Ref. 022377

4/3/15 (Item 15 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11681846 BIOSIS Number: 98281846
Activated T cells induce interleukin-12 production by monocytes via CD40-**CD40 ligand** interaction
Shu U; Kiniwa M; Wu C Y; Maliszewski C; Vezzio N; Hakimi J; Gately M; Delespesse G
Norte-Dame Hosp. Res. Cent., Allergy Res. Lab., 1560 Sherbrooke St. East, Montreal, PQ H2L 4M1, Canada
European Journal of Immunology 25 (4). 1995. 1125-1128.
Full Journal Title: European Journal of Immunology
ISSN: 0014-2980
Language: ENGLISH
Print Number: Biological Abstracts Vol. 100 Iss. 001 Ref. 006684

4/3/16 (Item 1 from file: 72)
DIALOG(R)File 72:EMBASE

10647882 EMBASE No: 98075646
CD40 Ligand /CD40 stimulation regulates the production of IFN-gamma from human peripheral blood mononuclear cells in an IL-12- and/or CD28-dependent manner
McDyer J.F.; Goletz T.J.; Thomas E.; June C.H.; Seder R.A.
Dr. J.F. McDyer, Laboratory of Clinical Investigation, Natl. Allergy/Infectious Dis. Inst., National Institutes of Health, Bethesda, MD 20892 United States
Journal of Immunology (United States) , 1998, 160/4 (1701-1707)
CODEN: JOIMA ISSN: 0022-1767
PUBLICATION DATE: 19980215
DOCUMENT TYPE: Journal Article
LANGUAGES: ENGLISH SUMMARY LANGUAGES: ENGLISH
NUMBER OF REFERENCES: 40

4/3/17 (Item 2 from file: 72)
DIALOG(R)File 72:EMBASE

10546511 EMBASE No: 97361587
Cytokines and immunity to viral infections
Ramshaw I.A.; Ramsay A.J.; Karupiah G.; Rolph M.S.; Mahalingam S.; Ruby J.C.
I.A. Ramshaw, Division Immunology and Cell Biology, John Curtin School Medical Research, Australian National University, Canberra, ACT 0200 Australia
Immunological Reviews (Denmark) , 1997, 159/- (119-135)
CODEN: IMRED ISSN: 0105-2896
DOCUMENT TYPE: Journal
LANGUAGES: English SUMMARY LANGUAGES: English
NUMBER OF REFERENCES: 96

4/3/18 (Item 3 from file: 72)
DIALOG(R)File 72:EMBASE
(c) 1998 Elsevier Science B.V. All rts. reserv.

10248993 EMBASE No: 97052669
Function and clinical use of interleukin-12
Trinchieri G.
USA
Current Opinion in Hematology (USA) , 1997, 4/1 (59-66)
CODEN: COHEF ISSN: 1065-6251
DOCUMENT TYPE: Journal
LANGUAGES: English SUMMARY LANGUAGES: English
NUMBER OF REFERENCES: 78

4/3/19 (Item 4 from file: 72)
DIALOG(R)File 72:EMBASE
(c) 1998 Elsevier Science B.V. All rts. reserv.

9978694 EMBASE No: 96166354
CD40-**CD40 ligand** interactions are critical in T-B cooperation but not for other anti-viral CD4+ T cell functions
Oxenius A.; Campbell K.A.; Maliszewski C.R.; Kishimoto T.; Kikutani H.; Hengartner H.; Zinkernagel R.M.; Bachmann M.F.
Institute of Experimental Immunology, Schmelzbergstr. 12, CH-8091 Zurich Switzerland
Journal of Experimental Medicine (USA) , 1996, 183/5 (2209-2218)
CODEN: JEMEA ISSN: 0022-1007
LANGUAGES: English SUMMARY LANGUAGES: English

4/3/20 (Item 5 from file: 72)
DIALOG(R)File 72:EMBASE
(c) 1998 Elsevier Science B.V. All rts. reserv.

9966357 EMBASE No: 96152206
Studying immunological tolerance by physically monitoring antigen-specific T cells in vivo
Khoruts A.; Jenkins M.K.
Department of Microbiology, University Minnesota Medical School, 420 Delaware Street SE, Minneapolis, MN 55455 USA
Annals of the New York Academy of Sciences (USA) , 1996, 778 (72-79)
CODEN: ANYAA ISSN: 0077-8923
LANGUAGES: English SUMMARY LANGUAGES: English

4/3/21 (Item 6 from file: 72)
DIALOG(R)File 72:EMBASE
(c) 1998 Elsevier Science B.V. All rts. reserv.

9594499 EMBASE No: 95163657
Getting to know you: Viruses meet **CD40 ligand**
McFadden G.
Department of Biochemistry, University of Alberta, Edmonton, Alta. T6G 2H7 Canada
Nature Medicine (USA) , 1995, 1/5 (408-409)
CODEN: NAMEF ISSN: 1078-8956
LANGUAGES: English

4/3/22 (Item 1 from file: 154)
DIALOG(R)File 154:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

09503173 98230457
IL-12 up-regulates **CD40 ligand** (CD154) expression on human T cells.
Peng X; Remacle JE; Kasran A; Huylebroeck D; Ceuppens JL
Department of Pathophysiology, Faculty of Medicine, Catholic University of Leuven, Belgium.
J Immunol (UNITED STATES) Feb 1 1998, 160 (3) p1166-72, ISSN 0022-1767 Journal Code: IFB
Languages: ENGLISH
Document type: JOURNAL ARTICLE

4/3/23 (Item 2 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09479030 98209743
Engagement of CD40 antigen with soluble **CD40 ligand** up-regulates peptide transporter expression and restores endogenous processing function in Burkitt's lymphoma cells.
Khanna R; Cooper L; Kienzle N; Moss DJ; Burrows SR; Khanna KK
EBV Unit, Queensland Institute of Medical Research, Herston, Australia. rajivK@qimr.edu.au
J Immunol (UNITED STATES) Dec 15 1997, 159 (12) p5782-5, ISSN 0022-1767 Journal Code: IFB
Contract/Grant No.: CA-52250-04, CA, NCI
Languages: ENGLISH
Document type: JOURNAL ARTICLE

4/3/24 (Item 3 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09479029 98209742
Immunostimulatory effects of a plasmid expressing **CD40 ligand** (CD154) on gene immunization.
Mendoza RB; Cantwell MJ; Kipps TJ
Human Gene Therapy Program, University of California-San Diego, La Jolla 92093-0663, USA.
J Immunol (UNITED STATES) Dec 15 1997, 159 (12) p5777-81, ISSN 0022-1767 Journal Code: IFB
Contract/Grant No.: CA66000, CA, NCI
Languages: ENGLISH
Document type: JOURNAL ARTICLE

4/3/25 (Item 4 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09438878 98161690
Generation and functional characterization of anti-clonotype antibodies to human T-cell receptors.
Steenbakkers PG; Boots AM; Rijnders AW
Department of Immunology, N.V. Organon, Oss, The Netherlands. p.steenbakkers@organon.oss.akzonobel.nl
J Immunol Methods (NETHERLANDS) Dec 15 1997, 210 (1) p51-64, ISSN 0022-1759 Journal Code: IFE
Languages: ENGLISH
Document type: JOURNAL ARTICLE

4/3/26 (Item 5 from file: 154)

DIALOG(R)File 154:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

08954468 97211840
Restoration of T cell-independent type 2 induction of Ig secretion by neonatal B cells in vitro.
Snapper CM; Rosas FR; Moorman MA; Mond JJ
Department of Pathology, Uniformed Services University of the Health Sciences, Bethesda, MD 20814, USA.
J Immunol (UNITED STATES) Mar 15 1997, 158 (6) p2731-5, ISSN 0022-1767 Journal Code: IFB
Contract/Grant No.: AI32560, AI, NIAID; AI36588, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE

4/3/27 (Item 6 from file: 154)
DIALOG(R)File 154:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

08864156 97131710
Antigen-driven but not lipopolysaccharide-driven IL-12 production in macrophages requires triggering of CD40.
DeKruyff RH; Gieni RS; Umetsu DT
Division of Immunology and Transplantation Biology, Department of Pediatrics, Stanford University, CA 94305, USA.
J Immunol (UNITED STATES) Jan 1 1997, 158 (1) p359-66, ISSN 0022-1767 Journal Code: IFB
Contract/Grant No.: RO1AI24571, AI, NIAID; RO1AI26322, AI, NIAID; KO7AI01026, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE

4/3/28 (Item 7 from file: 154)
DIALOG(R)File 154:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

08716999 96049696
Somatic mutation of human immunoglobulin V genes: bias, rate, and regulation.
Insel RA; Varade WS; Chu YW; Marin E; Fuleihan R; Geha RS
Department of Pediatrics, University of Rochester School of Medicine and Dentistry, New York 14642, USA.
Ann N Y Acad Sci (UNITED STATES) Sep 29 1995, 764 p158-69, ISSN 0077-8923 Journal Code: 5NM
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

4/3/29 (Item 8 from file: 154)
DIALOG(R)File 154:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

08526800 96140657
CD40-**CD40 ligand** interactions stimulate B cell antigen processing.
Faassen AE; Dalke DP; Berton MT; Warren WD; Pierce SK
Department of Biochemistry, Molecular Biology, Northwestern University, Evanston, IL 60208-3500, USA.
Eur J Immunol (GERMANY) Dec 1995, 25 (12) p3249-55, ISSN 0014-2980 Journal Code: EN5
Contract/Grant No.: F32 AI08884-01, AI, NIAID; AI27957, AI, NIAID; AI18939, AI, NIAID; +
Languages: ENGLISH

Document type: JOURNAL ARTICLE

4/3/30 (Item 9 from file: 154)
DIALOG(R)File 154:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

08426221 96010052
CD40 expression by human fibroblasts.
Fries KM; Sempowski GD; Gaspari AA; Blieden T; Looney RJ; Phipps RP
University of Rochester Cancer Center, University of Rochester School of Medicine and Dentistry, New York 14642, USA.
Clin Immunol Immunopathol (UNITED STATES) Oct 1995, 77 (1) p42-51, ISSN 0090-1229 Journal Code: DEA
Contract/Grant No.: CA55305, CA, NCI; CA42739, CA, NCI; CA11198, CA, NCI; +
Languages: ENGLISH
Document type: JOURNAL ARTICLE

4/3/31 (Item 10 from file: 154)
DIALOG(R)File 154:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

08415858 95332711
Cellular interaction in germinal centers. Roles of **CD40 ligand** and B7-2 in established germinal centers.
Han S; Hathcock K; Zheng B; Kepler TB; Hodes R; Kelsoe G
Department of Microbiology and Immunology, University of Maryland School of Medicine, Baltimore 21201, USA.
J Immunol (UNITED STATES) Jul 15 1995, 155 (2) p556-67, ISSN 0022-1767 Journal Code: IFB
Contract/Grant No.: AI-24335, AI, NIAID; AG-10207, AG, NIA
Languages: ENGLISH
Document type: JOURNAL ARTICLE

4/3/32 (Item 11 from file: 154)
DIALOG(R)File 154:MEDLINE(R)
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08018810 95008371
Collagen-induced arthritis as a model of rheumatoid arthritis.
Durie FH; Fava RA; Noelle RJ
Department of Microbiology, Dartmouth Medical School, Lebanon, New Hampshire 03756.
Clin Immunol Immunopathol (UNITED STATES) Oct 1994, 73 (1) p11-8, ISSN 0090-1229 Journal Code: DEA
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, ACADEMIC

4/3/33 (Item 12 from file: 154)
DIALOG(R)File 154:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

07817080 93369589
Prevention of collagen-induced arthritis with an antibody to **gp39**, the ligand for CD40.
Durie FH; Fava RA; Foy TM; Aruffo A; Ledbetter JA; Noelle RJ
Department of Microbiology, Dartmouth Medical School, Lebanon, NH 03756.
Science (UNITED STATES) Sep 3 1993, 261 (5126) p1328-30, ISSN 0036-8075 Journal Code: UJ7
Contract/Grant No.: AI26296, AI, NIAID
Languages: ENGLISH

Document type: JOURNAL ARTICLE

4/3/34 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

128139750 CA: 128(12)139750z PATENT
Method of activating dendritic cells
INVENTOR(AUTHOR): Maraskovsky, Eugene; Mckenna, Hilary R.
LOCATION: USA
ASSIGNEE: Immunex Corp.
PATENT: PCT International ; WO 9801538 A1 DATE: 19980115
APPLICATION: WO 97US11956 (19970709) *US 677762 (19960710) *US 763995 (19961212)
PAGES: 35 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-005/00A; C12N-015/63B; C12N-015/09B; A61K-048/00B DESIGNATED COUNTRIES: AU; CA; IL; JP; KR; MX; NO; NZ DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES; FI; FR; GB ; GR; IE; IT; LU; MC; NL; PT; SE

4/3/35 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

128101002 CA: 128(9)101002u JOURNAL
T-cell-mediated immunity against B-cell malignancies: preclinical results and translation into a novel immunotherapeutic approach for B-cell malignancies
AUTHOR(S): Schultze, J. L.
LOCATION: Dep. Adult Oncology, Dana-Farber Cancer Inst. & Dep. Medicine, Harvard medical School, Boston, MA, 02115, USA
JOURNAL: Haematol. Blood Transfus. DATE: 1998 VOLUME: 39 NUMBER: Acute Leukemias VII PAGES: 716-731 CODEN: HBTRDV ISSN: 0171-7111 LANGUAGE: English PUBLISHER: Springer-Verlag

4/3/36 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

128100826 CA: 128(9)100826d JOURNAL
Cutting edge: immunostimulatory effects of a plasmid expressing CD40 ligand (CD154) on gene immunization
AUTHOR(S): Mendoza, Robert B.; Cantwell, Mark J.; Kipps, Thomas J.
LOCATION: Human Gene Therapy Program, University California-San Diego, La Jolla, CA, 92093, USA
JOURNAL: J. Immunol. DATE: 1997 VOLUME: 159 NUMBER: 12 PAGES: 5777-5781 CODEN: JOIMA3 ISSN: 0022-1767 LANGUAGE: English PUBLISHER: American Association of Immunologists

4/3/37 (Item 4 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

128039547 CA: 128(4)39547v PATENT
Stimulation of immune response with low doses of interleukin-2
INVENTOR(AUTHOR): Smith, Kendall A.
LOCATION: USA
ASSIGNEE: Cornell Research Foundation, Inc.; Smith, Kendall A.
PATENT: PCT International ; WO 9741831 A1 DATE: 19971113
APPLICATION: WO 97US7787 (19970507) *US 646098 (19960507)
PAGES: 53 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-009/06A; A61K-009/08B; A61K-009/10B; A61K-009/107B; A61K-009/12B; A61K-009/127B;

A61K-009/14B; A61K-009/28B; A61K-009/40B; A61K-009/48B; A61K-009/52B; A61K-038/19B; A61K-038/20B; A61M-015/00B; A61M-015/08B; A61F-013/00B; A61K-009/70B DESIGNATED COUNTRIES: AL; AM; AT; AU; AZ; BB; BG; BR; BY; CA; CH; CN; CZ; DE; DK; EE; ES; FI; GB; GE; HU; IL; IS; JP; KE; KG; KP; KR; KZ; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; TJ; TM; TR; TT; UA; UG; US; UZ; VN; YU; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; KE; LS; MW; SD; SZ; UG; AT; BE; CH ; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE; SN; TD; TG

4/3/38 (Item 5 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

127233546 CA: 127(17)233546p PATENT
Methods and compositions for modulating an immune response
INVENTOR(AUTHOR): Armitage, Richard J.; Fanslow, William C.; Escobar, Carlos; Zappone, Jodee
LOCATION: USA
ASSIGNEE: Immunex Corporation
PATENT: PCT International ; WO 9729781 A1 DATE: 19970821
APPLICATION: WO 97US2350 (19970213) *US 601954 (19960215) *US 673753 (19960627) *US 720284 (19960926)
PAGES: 35 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-048/00A; C07K-005/00B; C07H-021/04B DESIGNATED COUNTRIES: AU; CA; NZ
DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE

4/3/39 (Item 6 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

127076013 CA: 127(6)76013t PATENT
Stimulation of antibody release by B lymphocytes with granulocyte-macrophage colony stimulating factor, interleukins, interferons, and universal T-cell epitopes
INVENTOR(AUTHOR): Mond, James J.; Snapper, Clifford M.
LOCATION: USA
ASSIGNEE: Henry M. Jackson Foundation for the Advancement of Military Medicine
PATENT: PCT International ; WO 9720940 A1 DATE: 19970612
APPLICATION: WO 96US19327 (19961205) *US 568343 (19951206)
PAGES: 60 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-015/62A; A61K-038/19B; A61K-038/20B; A61K-039/385B; A61K-039/44B
DESIGNATED COUNTRIES: AU; CA; JP DESIGNATED REGIONAL: AT; BE; CH; DE; DK ; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE

4/3/40 (Item 7 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

127049211 CA: 127(4)49211z PATENT
A semaphorin-like CD antigen, CD100, and a cDNA encoding it
INVENTOR(AUTHOR): Hall, Kathryn T.; Freeman, Gordon J.; Schultze, Joachim L.; Boussiotis, Vassiliki A.; Nadler, Lee M.
LOCATION: USA
ASSIGNEE: Dana-Farber Cancer Institute; Hall, Kathryn T.; Freeman, Gordon J.; Schultze, Joachim L.; Boussiotis, Vassiliki A.; Nadler, Lee M.
PATENT: PCT International ; WO 9717368 A1 DATE: 19970515
APPLICATION: WO 96US18645 (19961112) *US 556422 (19951109)
PAGES: 134 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07K-014/705A
DESIGNATED COUNTRIES: AU; CA; JP; US DESIGNATED REGIONAL: AT; BE; CH; DE

; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE

4/3/41 (Item 8 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 1998 American Chemical Society. All rts. reserv.

125284972 CA: 125(22)284972r PATENT
Compositions and methods for stimulating antibody class switching
INVENTOR(AUTHOR): Mond, James J.; Snapper, Clifford M.
LOCATION: USA
ASSIGNEE: Uniformed Services University of the Health Sciences
PATENT: PCT International ; WO 9627390 A1 DATE: 960912
APPLICATION: WO 96US2263 (960307) *US 400322 (950308)
PAGES: 42 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-039/385A; A61K-039/39B; A61K-038/20B; A61K-038/18B; A61K-038/17B; A61K-031/715B; A61K-039/385J; A61K-038/18J; A61K-038/17J; A61K-039/385K; A61K-038/17K; A61K-031/715K DESIGNATED COUNTRIES: AL; AM; AT; AU; AZ; BB; BG; BR; BY; CA ; CH; CN; CZ; DE; DK; EE; ES; FI; GB; GE; HU; IS; JP; KE; KG; KP; KR; KZ; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI DESIGNATED REGIONAL: KE; LS; MW; SD; SZ; UG; AT; BE; CH; DE; DK ; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML

4/3/42 (Item 9 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 1998 American Chemical Society. All rts. reserv.

125240241 CA: 125(19)240241x PATENT
Viral preparations, vectors, immunogens, and vaccines
INVENTOR(AUTHOR): Inglis, Stephen Charles; Boursnell, Michael Edward Griffith
LOCATION: UK,
ASSIGNEE: Cantab Pharmaceuticals Research Limited
PATENT: PCT International ; WO 9626267 A1 DATE: 960829
APPLICATION: WO 96GB385 (960221) *GB 953395 (950221) *GB 9515557 (950728) *GB 963322 (960216)
PAGES: 47 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-007/00A; C12N-015/86B; A61K-039/42B; C12N-005/00B; A61K-048/00B
DESIGNATED COUNTRIES: AU; CA; JP; US DESIGNATED REGIONAL: AT; BE; CH; DE ; DK; ES; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE

4/3/43 (Item 10 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 1998 American Chemical Society. All rts. reserv.

123141712 CA: 123(11)141712d PATENT
Compositions and method for stimulating antibody release by B lymphocytes
INVENTOR(AUTHOR): Snapper, Clifford M.; Mond, James J.
LOCATION: USA
ASSIGNEE: United States Dept. of the Army
PATENT: PCT International ; WO 9513089 A1 DATE: 950518
APPLICATION: WO 94US12802 (941108) *US 150510 (931110) *US 315492 (940930)
PAGES: 52 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-038/19A; C07K-017/10B; C07K-014/52B DESIGNATED COUNTRIES: AU; CA; JP
DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE

4/3/44 (Item 11 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 1998 American Chemical Society. All rts. reserv.

123132852 CA: 123(11)132852x PATENT
Treatment of viral disease with antigen-binding protein CD40-L
INVENTOR(AUTHOR): Ruby, Janet Caroline; Ramshaw, Ian Allister
LOCATION: Australia
ASSIGNEE: Australian National University
PATENT: PCT International ; WO 9514487 A1 DATE: 950601
APPLICATION: WO 94AU722 (941123) *AU 932587 (931124)
PAGES: 28 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-038/17A; C12N-007/01; C12N-015/12 DESIGNATED COUNTRIES: AU; JP; US
DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE

4/3/45 (Item 12 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

119093523 CA: 119(9)93523m PATENT
Murine and human cytokine (CD40-L) which binds to CD40, and soluble CD40 and CD40 fusion molecules
INVENTOR(AUTHOR): Armitage, Richard J.; Fanslow, William C.; Spriggs, Melanie K.
LOCATION: USA
ASSIGNEE: Immunex Corp.
PATENT: PCT International ; WO 9308207 A1 DATE: 930429
APPLICATION: WO 92US8990 (921023) *US 783707 (911025) *US 805723 (911205)
PAGES: 79 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07H-021/00A; A61K-035/14B; C07K-003/00B; C07K-007/00B; C07K-013/00B; C12P-021/02B; C12P-021/06B; C12N-015/00B DESIGNATED COUNTRIES: AU; CA; FI; JP; KR; NO
DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC; NL; SE

4/3/46 (Item 13 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

114227369 CA: 114(23)227369y PATENT
Immunogenic glycoproteins of human cytomegalovirus gCII complex, monoclonal antibodies to the glycoproteins, and use of the glycoproteins for a vaccine
INVENTOR(AUTHOR): Gehrz, Richard C.; Kari, Bruce E.
LOCATION: USA
ASSIGNEE: Children's Biomedical Research Center
PATENT: PCT International ; WO 9102004 A1 DATE: 910221
APPLICATION: WO 90US4371 (900803) *US 390300 (890807)
PAGES: 48 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07K-015/14A; A61K-039/00B DESIGNATED COUNTRIES: CA; JP DESIGNATED REGIONAL: AT; BE; CH ; DE; DK; ES; FR; GB; IT; LU; NL; SE

4/3/47 (Item 14 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

108050638 CA: 108(7)50638h PATENT
Polypeptide and nucleotide sequences of visna virus and their application in diagnostic assays and in production of immunogenic compositions
INVENTOR(AUTHOR): Sonigo, Pierre; Wain-Hobson, Simon
LOCATION: Fr.
ASSIGNEE: Institut Pasteur
PATENT: France Demande ; FR 2586427 A1 DATE: 870227
APPLICATION: FR 8512543 (850820)
PAGES: 27 pp. CODEN: FRXXBL LANGUAGE: French CLASS: C12N-015/00A;

C12N-005/00B; A61K-039/12B; A61K-037/02B; C07H-021/04B; C07K-007/10B; C07K-015/04B; C07K-015/14B; C12N-015/00J; C12R-001/91J

4/3/48 (Item 1 from file: 351)
DIALOG(R)File 351:DERWENT WPI

011684131
WPI Acc No: 98-101041/199809
XRAM Acc No: C98-033407
Activating antigen-expressing dendritic cells - useful to stimulate immune response to e.g. tumour, viral or bacterial antigens, as **vaccine adjuvant** and to produce antigen-specific T cells
Patent Assignee: IMMUNEX CORP (IMMV)
Inventor: MARASKOVSKY E; MCKENNA H R
Number of Countries: 025 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
WO 9801538	A1	19980115	WO 97US11956	A	19970709	C12N-005/00	199809 B

Priority Applications (No Type Date): US 96763995 A 19961212; US 96677762 A 19960710
Filing Details:

Patent	Kind	Filing Notes	Application	Patent
WO 9801538	A1			

Designated States (National): AU CA IL JP KR MX NO NZ
Designated States (Regional): AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Language, Pages: WO 9801538 (E, 35)

4/3/49 (Item 2 from file: 351)
DIALOG(R)File 351:DERWENT WPI

010305520 **Image available**
WPI Acc No: 95-206780/199527
XRAM Acc No: C95-095812
Treatment and prevention of viral infections with as e.g. HIV, herpes simplex virus or cytomegalovirus - using **CD40L** polypeptide or **vaccine**
Patent Assignee: UNIV AUSTRALIAN NAT (AUSU)
Inventor: RAMSHAW I A; RUBY J C
Number of Countries: 019 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
WO 9514487	A1	19950601	WO 94AU722	A	19941123	A61K-038/17	199527 B
AU 9510590	A	19950613	AU 9510590	A	19941123	A61K-038/17	199539

Priority Applications (No Type Date): AU 932587 A 19931124
Filing Details:

Patent	Kind	Filing Notes	Application	Patent
WO 9514487	A1			

Designated States (National): AU JP US
Designated States (Regional): AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE

AU 9510590	A	Based on	WO 9514487

Language, Pages: WO 9514487 (E, 28)

4/3/50 (Item 3 from file: 351)
DIALOG(R)File 351:DERWENT WPI

009796411
WPI Acc No: 94-076264/199410
XRAM Acc No: C94-034631
New nucleic acid encoding human **gp39** T cell antigen - which is a ligand for the CD40 receptor, causing proliferation and differentiation of B cells and some cancer cells
Patent Assignee: BRISTOL-MYERS SQUIBB CO (BRIM)
Inventor: ARUFFO A A; HOLLENBAUGH D; LEDBETTER J A; ARUFFO A; ARUFFO A E; HOLLEBAUGH D
Number of Countries: 026 Number of Patents: 014
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
EP 585943	A2	19940309	EP 93114153	A	19930903	C12N-015/12	199410 B
AU 9346120	A	19940310	AU 9346120	A	19930903	C12N-015/12	199415
NO 9303126	A	19940307	NO 933126	A	19930902	C07K-013/00	199416
CA 2105552	A	19940305	CA 2105552	A	19930903	C12N-015/12	199420
FI 9303862	A	19940305	FI 933862	A	19930903	C12N-015/28	199420
ZA 9306491	A	19940525	ZA 936491	A	19930902	A61K-000/00	199424
JP 6315383	A	19941115	JP 93243581	A	19930906	C12N-015/12	199505
EP 585943	A3	19940706				C12N-015/12	199528
HU 69977	T	19950928	HU 932484	A	19930903	C12N-015/12	199546
NZ 248569	A	19951026	NZ 248569	A	19930902	C12N-015/10	199604
US 5540926	A	19960730	US 92940605	A	19920904	A61K-039/395	199636
AU 677788	B	19970508	AU 9346120	A	19930903	C12N-015/12	199727
EP 585943	B1	19980211	EP 93114153	A	19930903	C12N-015/12	199811
DE 69316948	E	19980319	DE 616948	A	19930903	C12N-015/12	199817
			EP 93114153	A	19930903		

Priority Applications (No Type Date): US 92940605 A 19920904
Filing Details:

Patent	Kind	Filing Notes	Application	Patent
EP 585943	A2			
		Designated States (Regional): AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE		
AU 677788	B	Previous Publ.		AU 9346120
EP 585943	B1			
		Designated States (Regional): AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE		
DE 69316948	E	Based on		EP 585943

Language, Pages: EP 585943 (E, 39); ZA 9306491 (58); JP 6315383 (31); US

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 s (cd40)(20n)(antibod?)(20n)(adjuvant? or vaccin?)

            5612  CD40
         1035988  ANTIBOD?
           86286  ADJUVANT?
          195416  VACCIN?
      S5      24  (CD40)(20N)(ANTIBOD?)(20N)(ADJUVANT? OR VACCIN?)
? rd s5

>>>Duplicate detection is not supported for File 351.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
      S6      15  RD S5 (unique items)
? t s6/7/all


 6/7/1     (Item 1 from file: 55)
DIALOG(R)File  55:BIOSIS PREVIEWS(R)
(c) 1998 BIOSIS. All rts. reserv.

14153776     BIOSIS Number: 01153776
  Upregulation of CD40 ligand and IL-4 expression by the 23-valent
pneumococcal vaccine in children with recurrent infections
  Ortigas A P; Butler B; Leiva L E; Sorensen R U
  LSU Med. Cent., New Orleans, LA, USA
  Journal of Allergy and Clinical Immunology 101 (1 PART 2). 1998.  S15.
  Full Journal Title:  54th Annual Meeting of the American Academy of
Allergy, Asthma and Immunology, Washington, DC, USA, March 13-18, 1998.
Journal of Allergy and Clinical Immunology
  ISSN: 0091-6749
  Language: ENGLISH
  Print Number: Biological Abstracts/RRM Vol. 050 Iss. 004 Ref. 061660


 6/7/2     (Item 2 from file: 55)
DIALOG(R)File  55:BIOSIS PREVIEWS(R)
(c) 1998 BIOSIS. All rts. reserv.

13646832     BIOSIS Number: 99646832
  Protective immunity induced by tumor vaccines requires interaction
between CD40 and its ligand, CD154
  Mackey M F; Gunn J R; Ting P P; Kikutani H; Dranoff G; Noelle R J; Barth
R J Jr
  Sect. Gen. Surg., Dartmouth-Hitchcock Medical Cent., One Medical Center
Drive, Lebanon, NH 03756, USA
  Cancer Research 57 (13). 1997.  2569-2574.
  Full Journal Title:  Cancer Research
  ISSN: 0008-5472
  Language: ENGLISH
  Print Number: Biological Abstracts Vol. 104 Iss. 004 Ref. 055231
  Interactions  between CD40 and its ligand, CD154 (CD40L, gp39), have been
shown  to play a central role in the regulation of humoral immunity. Recent
evidence  suggests  that  this ligand-receptor pair also plays an important
role  in  the  induction of cell-mediated immune responses, including those
directed  against  viral  pathogens,  intracellular  parasites,  and
alloantigens.  The  contribution  of  this  ligand-receptor  pair  to  the
development  of  protective immunity against syngeneic tumors was evaluated
by  blocking  the in vivo function of CD154 or by studying tumor resistance
```

in mice genetically deficient in **CD40** expression (**CD40**-/-). In the former case, anti-CD154 monoclonal **antibody** treatment inhibited the generation of protective immune responses after the administration of three potent tumor **vaccines**: irradiated MCA 105, MCA 105 admixed with Corynebacterium parvum **adjuvant** , and irradiated B16 melanoma cells transduced with the gene for granulocyte macrophage colony-stimulating factor. Confirmation of the role of **CD40**/CD154 interactions in tumor immunity was provided by the overt tumor susceptibility in **CD40** -deficient mice as compared to that in CD40+/+ mice. In this case, wild-type but not CD40-deficient mice could be readily protected against live TS/A tumor challenge by preimmunization with TS/A admixed with C. parvum. These findings suggest a critical role for CD40/CD154 interactions in the induction of cellular immunity by tumor vaccines and may have important implications for future approaches to cell-based cancer therapies.

6/7/3 (Item 3 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

13619971 BIOSIS Number: 99619971
The role of diesel exhaust particles and their associated polyaromatic hydrocarbons in the induction of allergic airway disease
Diaz-Sanchez D
Hart and Louise Lyon Lab., Div. Clin. Immunol. and Allergy, Univ. Calif. Los Angeles Sch. Med., 10833 Le Conte Ave., 52-175 CHS, Los Angeles, CA 90024-1680, USA
Allergy (Copenhagen) 52 (SUPPL. 38). 1997. 52-56.
Full Journal Title: Allergy (Copenhagen)
ISSN: 0105-4538
Language: ENGLISH
Print Number: Biological Abstracts Vol. 104 Iss. 003 Ref. 045985
The increase in allergic airway disease has paralleled the increase in the use of fossil fuels. Studies were undertaken to examine whether extracts of polyaromatic hydrocarbons (PAH) from diesel exhaust particles (DEP) (PAH-DEP) acted as mucosal **adjuvants** to help initiate or enhance immunoglobulin E (IgE) production in response to common inhaled allergens. In vitro studies demonstrated that PAH-DEP enhanced IgE production by tonsillar B-cells in the presence of interleukin-4 (IL-4) and **CD40** monoclonal **antibody** , and altered the nature of the IgE produced, i.e. a decrease in the CH4'-CHe5 variant, a marker for differentiation of IgE-producing B-cells, and an increase in the M2' variant. In vivo nasal provocation studies using 0.30 mg DEP in saline also showed enhanced IgE production in the human upper respiratory mucosa, accompanied by a reduced CH4'-CHe5 mRNA splice variant. The effects of DEP were also isotype-specific, with no effect on IgG, IgA, IgM, or albumin, but it produced a small increase in the IgG-4 subclass. The ability of DEP to act as an adjuvant to the ragweed allergen Amb a I was examined by nasal provocation in ragweed allergic subjects using 0.3 mg DEP, Amb a I, or both. Although allergen and DEP each enhanced ragweed-specific IgE, DEP plus allergen promoted a 16-times greater antigen-specific IgE production. Nasal challenge with DEP also influenced cytokine production. Ragweed challenge resulted in a weak response, DEP challenge caused a strong but non-specific response, while allergen plus DEP caused a significant increase in the expression of mRNA for TH-0 and TH-2-type cytokines (IL-4, IL-5, IL-6, IL-10, IL-13) with a pronounced inhibitory effect on IFN-gamma gene expression. These studies suggest that DEP can enhance B-cell differentiation, and by initiating and elevating IgE production, may play an important role in the increased incidence of allergic airway disease.

6/7/4 (Item 4 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11714653 BIOSIS Number: 98314653
CD40 ligand has potent antiviral activity
Ruby J; Bluethmann H; Aguet M; Ramshaw I A
Viral Eng. Cytokines Group, Div. Cell Biol., John Curtin Sch. Med. Res., P.O. Box 334, Canberra 2601, Australia
Nature Medicine 1 (5). 1995. 437-441.
Full Journal Title: Nature Medicine
ISSN: 1078-8956
Language: ENGLISH
Print Number: Biological Abstracts Vol. 100 Iss. 002 Ref. 022377
For B cells to make **antibodies** against most antigens, they require help from T cells. T cell help is delivered as two signals to the B cell, one of which is via **CD40** and the other can be through receptors for any of a variety of soluble cytokines. We have constructed recombinant **vaccinia** viruses that express the ligand for **CD40** and have shown that the growth of these viruses is dramatically controlled in vivo, even in mice that lack T or B cells. In this paper, we also describe our attempts to analyse the **CD40** ligand-mediated antiviral activity by studying the clearance of these viruses in mice that are deficient in important antiviral mechanisms. Thus, the antiviral activity of CD40L may represent a surprising and potent effector mechanism of T cells activated during a virus infection.

6/7/5 (Item 5 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11108815 BIOSIS Number: 97308815
Lipopeptide-polyoxyethylene conjugates as mitogens and adjuvants
Kleine B; Rapp W; Wiesmueller K-H; Edinger M; Beck W; Metzger J; Ataulakhanov R; Jung G; Bessler W G
Institut fuer Immunobiologie, Stefan-Meier-Str.8, 79104 Freiburg, GER
Immunobiology 190 (1-2). 1994. 53-66.
Full Journal Title: Immunobiology
ISSN: 0171-2985
Language: ENGLISH
Print Number: Biological Abstracts Vol. 098 Iss. 002 Ref. 015327
Two lipopeptide analogues of the Escherichia coil lipoprotein rendered water-soluble by polyoxyethylene were tested for mitogenicity in vitro in murine and human B lymphocytes and for adjuvant activity in vivo in mice. These highly amphiphilic lipopeptides retained the biological activity Other lipopeptides usually exerted which supports the hypothesis of specific interactions of lipopeptides with membranes of reactive cells. The activation of human B lymphocytes by these lipopeptides was much less pronounced compared to that of murine cells. However, given in combination with anti-**CD40** **antibodies** plus interleukin-4, human B lymphocytes could synergistically be stimulated to proliferate. As an **adjuvant** , the polyoxyethylene linked lipopeptides were almost as potent as Freund's **adjuvants** and other basic lipopeptides. Being water-soluble, these novel analogues are easy to apply and they are suitable for field studies as adjuvants when sonication can not usually be provided.

6/7/6 (Item 1 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09479151 98189805
IgE versus IgG4 production can be differentially regulated by IL-10.
Jeannin P; Lecoanet S; Delneste Y; Gauchat JF; Bonnefoy JY
Geneva Biomedical Research Institute, Immunology Department, Glaxo Wellcome Research and Development SA, Switzerland.

J Immunol (UNITED STATES) Apr 1 1998, 160 (7) p3555-61, ISSN 0022-1767 Journal Code: IFB

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Allergen-specific IgE plays a key role in the physiopathology of allergic disorders. This IgE response is usually accompanied by a production of IgG4. Indirect evidence suggests that IgG4 may not be a sensitizing Ab but, in contrast, could be protective. As such, it may be of potential therapeutic interest to selectively modulate IgE vs IgG4 production. To date, IgE and IgG4 switching seems to be controlled by common mechanisms. We report here that IL-10 has a differential effect on IgE vs IgG4 production by PBMC. IL-10 decreases epsilon transcript expression and IgE production induced by IL-4 when added during the first 3 days of in vitro culture, suggesting that IL-10 decreases IL-4-induced IgE switching. In contrast, if added later on B cells that are already IgE switched, IL-10 potentiates IgE production. Interestingly, whatever the time of addition, IL-10 augments IL-4-induced gamma4 transcript expression and IgG4 production, with a maximal effect when added during the first 3 days. As IL-10 is not a switch factor for IgG4, it is likely that IL-10 enhances IgG4 production by potentiating IL-4-induced IgG4 switching. However, IL-10 may also act by enhancing the growth and/or differentiation of cells that are already IgG4 committed. Finally, CD40 ligation reverses the early down-regulating effect of IL-10 on IgE production. These results are the first evidence of a molecule that differentially regulates IgE vs IgG4 production, thereby suggesting the existence of a pathway(s) selectively controlling their production.

6/7/7 (Item 2 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09479029 98209742

Immunostimulatory effects of a plasmid expressing CD40 ligand (CD154) on gene immunization.

Mendoza RB; Cantwell MJ; Kipps TJ

Human Gene Therapy Program, University of California-San Diego, La Jolla 92093-0663, USA.

J Immunol (UNITED STATES) Dec 15 1997, 159 (12) p5777-81, ISSN 0022-1767 Journal Code: IFB

Contract/Grant No.: CA66000, CA, NCI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Interaction of CD40 with its ligand (CD154) can induce CD40-bearing APCs to express immune stimulatory accessory molecules that facilitate immune recognition. We evaluated whether a plasmid vector encoding CD154 (pCD40L) could influence the immune response to a transgene protein encoded by coinjected plasmid DNA. We found that coinjection of pCD40L in BALB/c mice enhanced the Ab response to beta-galactosidase induced by i.m. or intradermal injection of placZ, a plasmid DNA vector encoding beta-galactosidase. Furthermore, i.m. or intradermal coinjection of pCD40L with placZ enhanced the generation of CTL specific for P815 cells transfected with placZ. This study indicates that pCD40L can serve as a genetic adjuvant capable of augmenting humoral and cellular immune responses to Ags encoded by plasmid DNA expression vectors.

6/7/8 (Item 3 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09377119 98087484

Enhancement of T cell-independent immune responses in vivo by CD40 antibodies.

Dullforce P; Sutton DC; Heath AW

Division of Molecular and Genetic Medicine and Sheffield Institute for Vaccine Studies, University of Sheffield Medical School, UK.
Nat Med (UNITED STATES) Jan 1998, 4 (1) p88-91, ISSN 1078-8956
Journal Code: CG5
Languages: ENGLISH
Document type: JOURNAL ARTICLE

In this report we describe a potentially powerful method for vaccinating infants against encapsulated bacterial pathogens such as Haemophilus influenzae, Streptococcus pneumoniae and Neisseria meningitidis. High levels of antibody directed against the polysaccharides of the bacterial capsule are normally protective. Unfortunately, the capsular polysaccharides are T cell-independent antigens (TI); lacking T-cell help, they induce only weak, predominantly IgM antibody responses, with infants responding especially poorly. T-cell help, given to B cells during responses to protein antigens, causes stronger antibody responses and isotype switching to the IgG isotypes. T-cell help is mainly mediated through ligation of the B-cell surface antigen, CD40, by its cognate T-cell ligand, CD154. Here we show that administering anti-CD40 monoclonal antibody to mice, along with pneumococcal polysaccharide, provides a substitute for T-cell help and results in the generation of strong, isotype-switched antibody responses, which are protective. The work points the way toward a possible effective and inexpensive means of protecting susceptible groups against important bacterial pathogens.

6/7/9 (Item 4 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09329207 97461106
A function for CD2 on murine B cells?
Keogh MC; Elliot J; Norton T; Lake RA
Department of Immunology, St Mary's Hospital Medical School, Imperial College of Science, Technology and Medicine, London, UK.
Immunol Cell Biol (AUSTRALIA) Aug 1997, 75 (4) p333-9, ISSN 0818-9641
Journal Code: GH8
Languages: ENGLISH
Document type: JOURNAL ARTICLE

CD2 is expressed on murine B cells, probably as a result of a chromosomal translocation event during speciation. There are no activating antibodies to mouse CD2, but when activated non-specifically, only T cells up-regulate their expression of CD2. We investigated the expression and function of CD2 on B cells using mice transgenic for human CD2 under the control of a modified version of the autologous promoter/enhancer that included the immunoglobulin enhancer. This construction directs expression of human CD2 to the B cell compartment as well as to the T cell compartment. In this paper, we confirm that activating pairs of anti-CD2 monoclonal antibodies are mitogenic for mouse T cells transgenic for human CD2. In contrast, mouse B cells that express similar amounts of human CD2 are not stimulated to proliferate by equivalent doses of these antibodies. We were also unable to show any functional consequence for these B cells as a result of CD2 ligation.

6/7/10 (Item 5 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09214882 96067659
Differential regulatory effects of cAMP-elevating agents on human normal and neoplastic B cell functional response following ligation of surface immunoglobulin and CD40.
Kelly K; Knox KA
School of Biological and Molecular Sciences, Oxford Brookes University, United Kingdom.

Cell Immunol (UNITED STATES) Nov 1995, 166 (1) p93-102, ISSN 0008-8749 Journal Code: CQ9
Languages: ENGLISH
Document type: JOURNAL ARTICLE

The B cell response to ligation of surface immunoglobulin (sIg) and CD40 is dependent on the stage of cellular differentiation of the population studied. Cross-linking sIg promotes proliferation of follicular mantle (FM) B cells, rescues germinal center (GC) B cells from spontaneous apoptosis but induces apoptosis in susceptible Burkitt lymphoma (BL) B cells; signals transduced through CD40 induce resting FM B cells to enter cell cycle while promoting GC and BL B cell survival. This study investigates whether the 3', 5'-cyclic adenosine monophosphate (cAMP)-dependent second-messenger pathway plays a role in the regulation of these sIg- and CD40-promoted B cell responses, using prostaglandin E2 (PGE2) and forskolin to artificially increase intracellular levels of cAMP. The Epstein-Barr virus (EBV)-genome-negative BL B cell line Ramos is susceptible to growth arrest and apoptosis triggered by calcium ionophore, anti-IgM and forskolin but not by PGE2; forskolin does not affect the outcome of anti-IgM treatment. Anti-CD40 rescues Ramos-BL B cells from ionophore- and anti-IgM-triggered but not forskolin-triggered growth arrest and apoptosis; moreover, forskolin and anti-CD40 act additively and independently for enhanced growth inhibition. By contrast, both forskolin and PGE2 potentiate the proliferative response of FM B cells cultured with anti-Ig and anti-CD40 together but not individually. Forskolin and PGE2 fail to affect the spontaneous apoptosis and anti-Ig- and anti-CD40-promoted survival of GC B cells. Thus, the cAMP-dependent second messenger pathway can differentially influence the BL, FM, and GC B cell functional response to signals transduced through sIg and CD40.

6/7/11 (Item 6 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09162873 97439476

Interleukin-12 acts as an adjuvant for humoral immunity through interferon-gamma-dependent and -independent mechanisms.

Metzger DW; McNutt RM; Collins JT; Buchanan JM; Van Cleave VH; Dunnick WA
Department of Microbiology and Immunology, Medical College of Ohio, Toledo 43699-0008, USA. dmetzger@vortex.mco.edu

Eur J Immunol (GERMANY) Aug 1997, 27 (8) p1958-65, ISSN 0014-2980 Journal Code: EN5
Contract/Grant No.: AI94205, AI, NIAID; CA39068, CA, NCI
Languages: ENGLISH
Document type: JOURNAL ARTICLE

Interleukin-12 (IL-12) is a pivotal cytokine that has dramatic effects on cell-mediated immunity. It is now becoming increasingly recognized that IL-12 also strongly controls humoral immunity. We have investigated the mechanism by which IL-12 induces alterations in antibody isotype expression by determining the influence of IL-12 on in vitro immunoglobulin (Ig) production in polyclonally activated murine spleen cell cultures. Cells exposed to IL-12 plus lipopolysaccharide or anti-CD40 monoclonal antibody showed dramatically elevated IgG2a and suppressed IgG1 production compared to cells cultured in the absence of IL-12. IL-12 treatment of spleen cell cultures induced expression of gamma2a germ-line transcripts, consistent with initiation of switch recombination to IgG2a. In addition, exposure of limiting dilution cultures to IL-12 increased IgG2a+ cell precursor frequency. All of the above results were dependent on interferon-gamma (IFN-gamma). However, in the absence of IFN-gamma, IL-12 still had significant effects on Ig secretion. Specifically, IL-12 enhanced IgG1 and IgG2b anti-DNP antibody levels in mice containing specific disruptions in the IFN-gamma gene. Our results suggest that IL-12 induces T helper type 1 and natural killer cells to secrete large amounts of IFN-gamma which then causes B cells to switch to IgG2a and IgG3 production. In addition, IL-12 has direct or indirect effects on B cells that are independent of

IFN-gamma. The IFN-gamma-independent effects may include enhancement of Ig expression by post-switched cells.

6/7/12 (Item 7 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09107933 97376837
The effects of IFN-gamma on CD40-mediated activation of B cells from X-linked immunodeficient or normal mice.
Johnson-Leger C; Hasbold J; Holman M; Klaus GG
Division of Cellular Immunology, National Institute for Medical Research, London, United Kingdom.
J Immunol (UNITED STATES) Aug 1 1997, 159 (3) p1150-9, ISSN 0022-1767 Journal Code: IFB
Languages: ENGLISH
Document type: JOURNAL ARTICLE
B cell activation induced by cross-linking of CD40 is enhanced by costimulation with certain T cell-derived cytokines (generally Th2 type), most notably IL-4. We show here that the induction of DNA synthesis in normal mouse B cells by anti-CD40 mAb is also significantly enhanced by supernatants from anti-CD3-activated Th1 cells or from primary T cells. In both instances the costimulatory activity is specifically abrogated by neutralizing Abs against IFN-gamma. B cells from CBA/N immunodeficient (xid) mice are markedly hyporesponsive to most anti-CD40 Abs, even in the presence of IL-4. These cells do, however, synthesize DNA when stimulated by anti-CD40 plus supernatants from anti-CD3-stimulated primary T cells, by anti-CD40 plus IFN-gamma (but not IL-4), or by fixed, activated Th1 T cells. In all these instances, the mitogenic response of xid B cells is crucially dependent on the presence of IFN-gamma. This cytokine also enhanced CD40-induced homotypic adhesion of normal and xid B cells and potentiated CD40-mediated protection of B cells from spontaneous apoptosis. These data, therefore, indicate that IFN-gamma plays an essential role in the activation of B cells by Th1 T cells and by naive T cells during the initiation of primary Ab responses. The results with CBA/N B cells further suggest that the xid mutation selectively affects their capacity to respond to Th2-derived signals, for reasons that remain unclear.

6/7/13 (Item 8 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

08724306 96228274
T-independent activation of B cells by vesicular stomatitis virus: no evidence for the need of a second signal.
Fehr T; Bachmann MF; Bluethmann H; Kikutani H; Hengartner H; Zinkernagel RM
Institute of Experimental Immunology, University of Zurich, Switzerland.
Cell Immunol (UNITED STATES) Mar 15 1996, 168 (2) p184-92, ISSN 0008-8749 Journal Code: CQ9
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Vesicular stomatitis virus (VSV) induces a T helper cell-independent IgM antibody response, whereas the IgG response is strictly T helper cell dependent. Since VSV induces B cells in complete absence of T helper cells, the question arises as to whether this induction occurs in the absence of a second signal or whether it depends upon an alternative or replacing signal 2. We therefore asked whether VSV has polyclonal B cell stimulator activity and/or whether B cell induction by VSV needs costimulation via complement or tumor necrosis factor (TNF) receptor or by natural killer (NK) cell activity. In vitro B cell proliferation assays and analysis of the in vivo antibody response in CD40-deficient mice excluded that VSV has properties of a polyclonal B cell stimulator. C3 depletion by cobra venom factor and

application of anti-complement receptor antibodies showed that the T-independent IgM response was largely C3-independent except under very limiting antigen doses. Immunization of TNF receptor-deficient mice showed a normal anti-VSV IgM response, and in a cytotoxicity assay on YAC target cells there was no evidence of NK cell activation by VSV. Thus, VSV seems to induce B cells without polyclonal activation and/or C3, TNF, or NK cells functioning as a replacing second signal.

6/7/14 (Item 9 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

08526800 96140657
CD40-CD40 ligand interactions stimulate B cell antigen processing.
Faassen AE; Dalke DP; Berton MT; Warren WD; Pierce SK
Department of Biochemistry, Molecular Biology, Northwestern University, Evanston, IL 60208-3500, USA.
Eur J Immunol (GERMANY) Dec 1995, 25 (12) p3249-55, ISSN 0014-2980 Journal Code: EN5
Contract/Grant No.: F32 AI08884-01, AI, NIAID; AI27957, AI, NIAID; AI18939, AI, NIAID; +
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The interactions between B cell CD40 and T cell CD40 ligand (CD40L) have been shown recently to play an important role in T cell-dependent activation of B cells. Here, we show that the ligation of CD40 stimulates the processing of antigen by B cells. The activation of an antigen-specific T cell hybrid by B cells co-cultured with insect cells expressing recombinant CD40L or with a CD40-specific monoclonal antibody requires less antigen and fewer B cells compared to control cells. The augmentation was observed both for processing initiated by antigen binding to and cross-linking the surface immunoglobulin, and processing of antigen taken up by fluid-phase pinocytosis. CD40 appears to affect a step in the intracellular processing of antigen, as CD40 has no effect on the presentation of an antigenic peptide which does not require processing. In addition, the CD40-induced augmentation of processing is not attributable to the effect of CD40 ligation on the cell surface expression of B7, LFA-1 or CD23. CD40 ligation does not affect the biosynthesis of the class II EK molecules, and although ligation of CD40 induces B cell proliferation, the augmentation of processing does not require proliferation. The ability of CD40 to stimulate B cell antigen processing has the potential to influence significantly the outcome of antigen-dependent T cell-B cell interactions.

6/7/15 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

119093523 CA: 119(9)93523m PATENT
Murine and human cytokine (CD40-L) which binds to CD40, and soluble CD40 and CD40 fusion molecules
INVENTOR(AUTHOR): Armitage, Richard J.; Fanslow, William C.; Spriggs, Melanie K.
LOCATION: USA
ASSIGNEE: Immunex Corp.
PATENT: PCT International ; WO 9308207 A1 DATE: 930429
APPLICATION: WO 92US8990 (921023) *US 783707 (911025) *US 805723 (911205)
PAGES: 79 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07H-021/00A; A61K-035/14B; C07K-003/00B; C07K-007/00B; C07K-013/00B; C12P-021/02B; C12P-021/06B; C12N-015/00B DESIGNATED COUNTRIES: AU; CA; FI; JP; KR; NO
DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC; NL; SE
SECTION:
CA215005 Immunochemistry

CA201XXX Pharmacology
IDENTIFIERS: CD40 ligand cytokine, DNA cloning CD40 ligand cytokine, Fc CD40 fusion protein prodn, sequence CD40 ligand DNA
DESCRIPTORS:
Translation,genetic...
(antisense) oligonucleotides for inhibition of, of CD40 ligand cytokine
Transcription,genetic...
(antisense) oligonucleotides for inhibition of, of CD40 ligand cytokine nucleic acid
Genetic vectors...
cDNA for CD40 ligand cytokine on
Allergy inhibitors... Inflammation inhibitors,antirheumatics...
CD40 antagonist polypeptides for
Membrane,biological...
CD40 ligand bound to, as adjuvant for vaccine response augmentation and for stimulation of monoclonal antibody secretion by hybridoma
Lymphocyte,B-cell...
CD40 ligand cytokine effect on proliferation of and antibody prodn. by
Animal cell line,EL4...
CD40 ligand expression in
Immunostimulants,adjuvants...
CD40 ligand polypeptides as
Antigens,CD40...
cytokine ligand binding to
Deoxyribonucleic acid sequences...
for CD40 ligand cytokine, of human and mouse
Nucleotides,oligo-,polymers...
for transcription/translation inhibition of CD40 ligand cytokine
Immunoglobulins,A... Immunoglobulins,E... Immunoglobulins,G1...
Immunoglobulins,G2b... Immunoglobulins,G3... Immunoglobulins,M...
formation of, CD40 ligand cytokine effect on
Molecular cloning...
of cDNA for CD40 ligand cytokine
Proteins,specific or class, fusion products...
of CD40 and IgG1 Fc sequences, recombinant prodn. and therapeutic use of
Protein sequences...
of CD40 ligand cytokine, of human and mouse
Immunoglobulins,E, Fc.epsilon.RII receptors... Receptors,Fc.epsilon.RII (IgE fragment Fc receptor II)...
sol., interleukin-4-induced shedding of, from B-cells, inhibition of, by sol. CD40 mol. and CD40/Fc fusion protein
Antibodies... Antibodies,monoclonal...
to CD40 ligand cytokine
Lupus erythematosus... Transplant and Transplantation,graft-vs.-host reaction...
treatment of, CD40 antagonist polypeptides for
CAS REGISTRY NUMBERS:
149119-84-6 149119-85-7 149119-86-8 149119-89-1 149119-93-7 amino acid sequence of
149119-87-9 149119-92-6 nucleotide sequence of
149119-88-0 nucleotide sequence of and cloning of
149119-90-4 149119-91-5 nucleotide sequence of, CD40/Fc fusion protein construction in relation to

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 ds

Set     Items   Description
S1         29   (CD40L OR CD40(W)LIGAND OR 5C8 OR GP39)(20N)(VACCIN? OR AD-
               JUVANT?)
S2         22   RD S1 (unique items)
S3         81   (CD40L OR CD40(W)LIGAND OR GP39 OR 5C8) AND (VACCIN? OR AD-
               JUVANT?)
S4         50   RD S3 (unique items)
S5         24   (CD40)(20N)(ANTIBOD?)(20N)(ADJUVANT? OR VACCIN?)
S6         15   RD S5 (unique items)
? s (s3 or s5) and independent

             81  S3
             24  S5
         433771  INDEPENDENT
      S7     14  (S3 OR S5) AND INDEPENDENT
? rd s7

>>>Duplicate detection is not supported for File 351.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
      S8      9  RD S7 (unique items)
? t s8/7/all


 8/7/1     (Item 1 from file: 55)
DIALOG(R)File  55:BIOSIS PREVIEWS(R)
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13185422     BIOSIS Number: 99185422
  Differential activation requirements of isotype-switched B cells
  Ehrhardt R O; Harriman G R; Inman J K; Lycke N; Gray B; Strober W
  Mucosal Immunity Sect., LCI, NIAID, Natl. Inst. Health, Bethesda, MD
20892, USA
  European Journal of Immunology 26 (8). 1996.  1926-1934.
  Full Journal Title:  European Journal of Immunology
  ISSN: 0014-2980
  Language: ENGLISH
  Print Number: Biological Abstracts Vol. 102 Iss. 008 Ref. 117429
  In the present studies, we compared the activation requirements of
sIgM+/sIgD+ B cells with those of isotype-switched sIgM-/sIgA+ B cells. We
found that whereas sIgM+ B cells respond to T cell-independent (TI)
and T cell-dependent (TD) Ag with no significant bias toward one stimulus,
sIgA+ B cells were deficient in their ability to respond to antigen
receptor cross-linking but responded remarkably well to TD stimuli. Thus,
dextran-conjugated anti-IgA antibody (anti-IgA-dextran), anti-kappa-dextran
, or various immobilized anti-IgA antibodies (Ab) induced only low-level
IgA B cell proliferation and no IgA secretion in the presence of various
lymphokines, in marked contrast, sIgA+ B cells responded to cognate and
noncognate T cell stimulation as well as to stimulation by CD40
ligand -bearing fibroblasts by secreting large amounts of IgA (up to
240 000 ng/ml per 10-5 cells). This pattern of sIgA+ B cell responsiveness
was noted with both germinal center peanut agglutinin-hi (PNA-hi) and
non-germinal center PNA-lo B cells. In confirmation of these results, whole
Peyer's patch or lamina propria cell populations containing less than 15%
sIgA+ B cells stimulated with a noncognate T cell stimulus or T cell
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membranes secreted mainly IgA (68%-94% of the total Ig secreted) and relatively little IgM. The strict T cell dependence of IgA B cell activation and differentiation provides important insights into immune responses of mucosal tissues and must be considered in the development of **vaccines** , particularly those designed to stimulate mucosal tissues containing large numbers of isotype-switched B cells.

8/7/2 (Item 1 from file: 72)
DIALOG(R)File 72:EMBASE

10647882 EMBASE No: 98075646
CD40 Ligand /CD40 stimulation regulates the production of IFN-gamma from human peripheral blood mononuclear cells in an IL-12- and/or CD28-dependent manner
McDyer J.F.; Goletz T.J.; Thomas E.; June C.H.; Seder R.A.
Dr. J.F. McDyer, Laboratory of Clinical Investigation, Natl. Allergy/Infectious Dis. Inst., National Institutes of Health, Bethesda, MD 20892 United States
Journal of Immunology (United States) , 1998, 160/4 (1701-1707)
CODEN: JOIMA ISSN: 0022-1767
PUBLICATION DATE: 19980215
DOCUMENT TYPE: Journal Article
LANGUAGES: ENGLISH SUMMARY LANGUAGES: ENGLISH
NUMBER OF REFERENCES: 40
CD40 ligand (**CD40L**)/CD40 costimulation is an important regulator of Th1 responses. Two mechanisms by which **CD40L**/CD40 stimulation may enhance IFN-gamma are via direct induction of IL-12 and augmentation of the expression of costimulatory molecules such as B7 from APCs. We examined the ability of **CD40L**/CD40 stimulation to regulate the production of IFN-gamma through IL-12 and/or CD28 costimulation from human PBMCs stimulated with T cell-specific stimuli. The roles of exogenous and endogenous **CD40L**/CD40 stimulation were evaluated using trimetric soluble **CD40L** agonist (CD40T) and an anti-**CD40L** Ab, respectively. The presence of CD40T in cultures increased the production of IL-12 and IFN-gamma from PBMCs stimulated with varying amounts of PHA. The mechanism, however, by which CD40T enhanced IFN-gamma varied according to the level of T cell activation. Under maximal stimulator conditions (PHA, 1/100), an IL-12-dependent was dominant. At relatively low levels of T cell stimulation (PHA, 1/500 and 1/1000) however, an additional IL-12-**independent** pathway was elucidated. We further studied the role of exogenous CD28 stimulation in regulating the production of IFN-gamma. The enhancement of IFN- gamma production induced by direct CD28 stimulation was primarily dependent on endogenous IL-12 or **CD40L**/CD40 stimulation. Together, these data suggest that the production of IFN-gamma involves a complex interaction between two interdependent, yet distinct, costimulatory pathways and provide evidence that CD40T may be an effective **adjuvant** for the enhancement of responses.

8/7/3 (Item 2 from file: 72)
DIALOG(R)File 72:EMBASE

10248993 EMBASE No: 97052669
Function and clinical use of interleukin-12
Trinchieri G.
USA
Current Opinion in Hematology (USA) , 1997, 4/1 (59-66)
CODEN: COHEF ISSN: 1065-6251
DOCUMENT TYPE: Journal
LANGUAGES: English SUMMARY LANGUAGES: English
NUMBER OF REFERENCES: 78
Interleukin-12 is a heterodimeric cytokine produced by phagocytic cells,

professional antigen-presenting cells such as dendritic cells and skin Langerhans cells, and B cells. Interleukin-12 production is induced by bacteria, intracellular pathogens, fungi, viruses, or their products in a T- cell-**independent** pathway or a T-cell-dependent pathway, the latter mediated through **CD40 ligand**-CD40 interaction. Interleukin-12 is produced rapidly after infection and acts as a proinflammatory cytokine eliciting production of interferon gamma, by T and natural killer cells, which activates phagocytic cells. The production of interleukin-12 is strictly regulated by positive and negative feedback mechanisms. If interleukin-12 and interleukin- 12-induced interferon gamma are present during early T-cell expansion in response to antigen, T-helper type-1 cell generation is favored and generation of T-helper type-2 cells is inhibited. Thus interleukin-12 is also a potent immunoregulatory cytokine that promotes T-helper type-1 differentiation and is instrumental in the T-helper type-1-dependent resistance to infections by bacteria, intracellular parasites, fungi, and certain viruses. By inhibiting T-helper type-2 cell response, interleukin-12 has a suppressive effect on allergic reactions; by promoting T-helper type-1 responses it participates in the immunopathology responsible for several organ-specific autoimmune diseases. Viruses inducing a permanent or transient immunodepression, such as HIV and measles, may act, in part, by suppressing interleukin-12 production. Because of its ability to enhance resistance to several infectious diseases and to act as an **adjuvant** in **vaccination**, and because of its powerful antitumor effect in vivo, interleukin-12 is currently in clinical trials in cancer patients and HIV-infected patients, and it is being considered for therapeutic use in other diseases.

8/7/4 (Item 1 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09377119 98087484
Enhancement of T cell-**independent** immune responses in vivo by CD40 antibodies.
Dullforce P; Sutton DC; Heath AW
Division of Molecular and Genetic Medicine and Sheffield Institute for Vaccine Studies, University of Sheffield Medical School, UK.
Nat Med (UNITED STATES) Jan 1998, 4 (1) p88-91, ISSN 1078-8956
Journal Code: CG5
Languages: ENGLISH
Document type: JOURNAL ARTICLE
In this report we describe a potentially powerful method for vaccinating infants against encapsulated bacterial pathogens such as Haemophilus influenzae, Streptococcus pneumoniae and Neisseria meningitidis. High levels of antibody directed against the polysaccharides of the bacterial capsule are normally protective. Unfortunately, the capsular polysaccharides are T cell-**independent** antigens (TI); lacking T-cell help, they induce only weak, predominantly IgM antibody responses, with infants responding especially poorly. T-cell help, given to B cells during responses to protein antigens, causes stronger antibody responses and isotype switching to the IgG isotypes. T-cell help is mainly mediated through ligation of the B-cell surface antigen, CD40, by its cognate T-cell ligand, CD154. Here we show that administering anti-CD40 monoclonal antibody to mice, along with pneumococcal polysaccharide, provides a substitute for T-cell help and results in the generation of strong, isotype-switched antibody responses, which are protective. The work points the way toward a possible effective and inexpensive means of protecting susceptible groups against important bacterial pathogens.

8/7/5 (Item 2 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09162873 97439476
Interleukin-12 acts as an adjuvant for humoral immunity through interferon-gamma-dependent and **-independent** mechanisms.
Metzger DW; McNutt RM; Collins JT; Buchanan JM; Van Cleave VH; Dunnick WA
Department of Microbiology and Immunology, Medical College of Ohio, Toledo 43699-0008, USA. dmetzger@vortex.mco.edu
Eur J Immunol (GERMANY) Aug 1997, 27 (8) p1958-65, ISSN 0014-2980
Journal Code: EN5
Contract/Grant No.: AI94205, AI, NIAID; CA39068, CA, NCI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Interleukin-12 (IL-12) is a pivotal cytokine that has dramatic effects on cell-mediated immunity. It is now becoming increasingly recognized that IL-12 also strongly controls humoral immunity. We have investigated the mechanism by which IL-12 induces alterations in antibody isotype expression by determining the influence of IL-12 on in vitro immunoglobulin (Ig) production in polyclonally activated murine spleen cell cultures. Cells exposed to IL-12 plus lipopolysaccharide or anti-CD40 monoclonal antibody showed dramatically elevated IgG2a and suppressed IgG1 production compared to cells cultured in the absence of IL-12. IL-12 treatment of spleen cell cultures induced expression of gamma2a germ-line transcripts, consistent with initiation of switch recombination to IgG2a. In addition, exposure of limiting dilution cultures to IL-12 increased IgG2a+ cell precursor frequency. All of the above results were dependent on interferon-gamma (IFN-gamma). However, in the absence of IFN-gamma, IL-12 still had significant effects on Ig secretion. Specifically, IL-12 enhanced IgG1 and IgG2b anti-DNP antibody levels in mice containing specific disruptions in the IFN-gamma gene. Our results suggest that IL-12 induces T helper type 1 and natural killer cells to secrete large amounts of IFN-gamma which then causes B cells to switch to IgG2a and IgG3 production. In addition, IL-12 has direct or indirect effects on B cells that are **independent** of IFN-gamma. The IFN-gamma-**independent** effects may include enhancement of Ig expression by post-switched cells.

8/7/6 (Item 3 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

08954468 97211840
Restoration of T cell-**independent** type 2 induction of Ig secretion by neonatal B cells in vitro.
Snapper CM; Rosas FR; Moorman MA; Mond JJ
Department of Pathology, Uniformed Services University of the Health Sciences, Bethesda, MD 20814, USA.
J Immunol (UNITED STATES) Mar 15 1997, 158 (6) p2731-5, ISSN 0022-1767 Journal Code: IFB
Contract/Grant No.: AI32560, AI, NIAID; AI36588, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The humoral immune response of neonates to T cell-**independent** type 2 (TI-2) Ags is markedly defective. We previously demonstrated that multivalent membrane Ig cross-linking, using dextran-conjugated anti-Ig Abs (anti-Ig-dextran), is an in vitro model for membrane Ig-dependent TI-2 induction of Ig secretion. In this work, we demonstrate that highly purified neonatal B cells are intrinsically defective in IgM secretion in response to anti-Ig-dextran and cytokines in vitro, as well as other modes of B cell activation, relative to adult B cells. However, costimulation of anti-Ig-dextran-activated neonatal B cells with either **CD40-ligand** , a recombinant bacterial lipoprotein, or LPS restores the IgM secretory response of neonatal B cells to adult levels. Analysis of Ig isotype secretion indicates that neonatal B cells have an enhanced capacity to secrete IgE and IgA relative to other Ig isotypes. These data suggest that neonatal B cells are competent to secrete Ig in response to TI-2 Ags if adequate costimuli are provided, and thus may have particular relevance

for the design of **vaccine** strategies in the immunodeficient host. The data also suggest that neonatal B cells are programmed to secrete relatively enhanced amounts of IgE and IgA, which may be relevant for antimicrobial resistance at mucosal surfaces.

8/7/7 (Item 4 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

08864156 97131710
Antigen-driven but not lipopolysaccharide-driven IL-12 production in macrophages requires triggering of CD40.
DeKruyff RH; Gieni RS; Umetsu DT
Division of Immunology and Transplantation Biology, Department of Pediatrics, Stanford University, CA 94305, USA.
J Immunol (UNITED STATES) Jan 1 1997, 158 (1) p359-66, ISSN 0022-1767 Journal Code: IFB
Contract/Grant No.: RO1AI24571, AI, NIAID; RO1AI26322, AI, NIAID; KO7AI01026, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We demonstrated that two distinct pathways exist for the induction of IL-12 in APC. The first pathway for IL-12 production occurred during responses to T cell-dependent Ags such as OVA and required triggering of CD40 molecules on the APC. IL-12 production in this T cell-dependent system increased in direct proportion to Ag concentration and required TCR ligation but not CD28 costimulation. The second pathway occurred when bacterial products such as LPS or heat-killed Listeria monocytogenes were used to activate macrophages to produce IL-12 in the complete absence of T cells. In this second pathway, IL-12 production was completely **independent** of CD40 triggering. In both pathways, the presence of IFN-gamma was not required for induction of IL-12 synthesis when splenic adherent cells (SAC) from normal mice were used. However, addition of IFN-gamma to cultures of Th2 T cells and SAC increased IL-12 production two- to fivefold, and addition of rTNF-alpha with IFN-gamma further enhanced IL-12 production. The addition of TNF-alpha in the absence of IFN-gamma, however, had no effect on IL-12 production in the T cell-dependent pathway. Similarly, addition of TNF-alpha in the presence or the absence of IFN-gamma to cultures of LPS or heat-killed Listeria and SAC did not increase IL-12 production, but addition of IFN-gamma alone greatly enhanced IL-12 production, consistent with the idea that bacterial stimuli induce significant quantities of endogenous TNF-alpha production. These results indicate that the requirements for the induction of IL-12 production in T cell-dependent and T cell-**independent** responses differs mainly with regard to CD40 triggering. Furthermore, these results suggest that IL-12 production can be induced by bacterial products in patients with hyper-IgM syndrome who lack **CD40 ligand** expression and in those treated with soluble **gp39** to interrupt CD40-**CD40 ligand** interactions.

8/7/8 (Item 5 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

08724306 96228274
T-**independent** activation of B cells by vesicular stomatitis virus: no evidence for the need of a second signal.
Fehr T; Bachmann MF; Bluethmann H; Kikutani H; Hengartner H; Zinkernagel RM
Institute of Experimental Immunology, University of Zurich, Switzerland.
Cell Immunol (UNITED STATES) Mar 15 1996, 168 (2) p184-92, ISSN 0008-8749 Journal Code: CQ9
Languages: ENGLISH

Document type: JOURNAL ARTICLE

Vesicular stomatitis virus (VSV) induces a T helper cell-**independent** IgM antibody response, whereas the IgG response is strictly T helper cell dependent. Since VSV induces B cells in complete absence of T helper cells, the question arises as to whether this induction occurs in the absence of a second signal or whether it depends upon an alternative or replacing signal 2. We therefore asked whether VSV has polyclonal B cell stimulator activity and/or whether B cell induction by VSV needs costimulation via complement or tumor necrosis factor (TNF) receptor or by natural killer (NK) cell activity. In vitro B cell proliferation assays and analysis of the in vivo antibody response in CD40-deficient mice excluded that VSV has properties of a polyclonal B cell stimulator. C3 depletion by cobra venom factor and application of anti-complement receptor antibodies showed that the T-**independent** IgM response was largely C3-**independent** except under very limiting antigen doses. Immunization of TNF receptor-deficient mice showed a normal anti-VSV IgM response, and in a cytotoxicity assay on YAC target cells there was no evidence of NK cell activation by VSV. Thus, VSV seems to induce B cells without polyclonal activation and/or C3, TNF, or NK cells functioning as a replacing second signal.

8/7/9 (Item 6 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

08415858 95332711

Cellular interaction in germinal centers. Roles of **CD40 ligand** and B7-2 in established germinal centers.

Han S; Hathcock K; Zheng B; Kepler TB; Hodes R; Kelsoe G

Department of Microbiology and Immunology, University of Maryland School of Medicine, Baltimore 21201, USA.

J Immunol (UNITED STATES) Jul 15 1995, 155 (2) p556-67, ISSN 0022-1767 Journal Code: IFB

Contract/Grant No.: AI-24335, AI, NIAID; AG-10207, AG, NIA

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Costimulatory interactions between T and B lymphocytes are crucial for T cell activation and B cell proliferation and differentiation. We have compared the roles of **CD40L** and B7-2 in the initiation and maturation of humoral immunity by administering anti-**CD40 ligand** (L) or anti-B7-2 Ab during the early (days -1 to 3) or late (days 6-10) phases of primary responses to thymus-dependent (Td) and -**independent** (Ti) Ags. Germinal center (GC) formation in response to a Td Ag was inhibited completely by the early administration of anti-**CD40L** or anti-B7-2 Abs. Later in the response, established GCs remained sensitive to anti-**CD40L** but were resistant to treatment with anti-B7-2. However, Ig hypermutation was reduced dramatically in GCs of anti-B7-2-treated mice and humoral memory was impaired. Early administration of anti-**CD40L** reduced serum Ab levels to approximately 10% of controls, whereas early treatment with anti-B7-2 reduced Ab production by only 50%. Later treatments with either Ab had no effect on Ab production. Response to a type II Ti Ag was more resistant than Td responses to interruption of costimulatory interactions. Our findings suggest that the costimulatory roles of CD40:**CD40L** and B7-2:CD28/CTLA-4 differ in the GC; administration of anti-**CD40L** abrogates an established GC reaction, whereas Ab to B7-2 suppresses Ig hypermutation and entry into the B cell memory compartment. Once B cells have entered the differentiation pathway to Ab production, neither **CD40L** nor B7-2 is necessary for their continued differentiation and persistence.

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Ref    Items  Index-term
E1         2  AU=HEATFIELD, B. M.
E2         9  AU=HEATFIELD, BARRY M.
E3         1 *AU=HEATH
E4       116  AU=HEATH A
E5        34  AU=HEATH A B
E6       147  AU=HEATH A C
E7        24  AU=HEATH A C G
E8         3  AU=HEATH A D
E9         1  AU=HEATH A E
E10        3  AU=HEATH A E F
E11        1  AU=HEATH A F
E12       20  AU=HEATH A G

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Ref    Items  Index-term
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E14        1  AU=HEATH A K
E15        2  AU=HEATH A L
E16        1  AU=HEATH A M
E17       12  AU=HEATH A R
E18        3  AU=HEATH A S
E19        2  AU=HEATH A T
E20       48  AU=HEATH A W
E21       44  AU=HEATH A.
E22       27  AU=HEATH A.B.
E23       99  AU=HEATH A.C.
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E32        7  AU=HEATH A.R.
E33        3  AU=HEATH A.S.
E34        1  AU=HEATH A.T.
E35       27  AU=HEATH A.W.
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E48        7  AU=HEATH AR

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E6         4  AU=HEATH, ANDREW E.
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E11        1  AU=HEATH, ANDREW WILLIAM
E12        1  AU=HEATH, ARCHIE D.

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Set     Items   Description
S1         29   (CD40L OR CD40(W)LIGAND OR 5C8 OR GP39)(20N)(VACCIN? OR AD-
               JUVANT?)
S2         22   RD S1 (unique items)
S3         81   (CD40L OR CD40(W)LIGAND OR GP39 OR 5C8) AND (VACCIN? OR AD-
               JUVANT?)
S4         50   RD S3 (unique items)
S5         24   (CD40)(20N)(ANTIBOD?)(20N)(ADJUVANT? OR VACCIN?)
S6         15   RD S5 (unique items)
S7         14   (S3 OR S5) AND INDEPENDENT
S8          9   RD S7 (unique items)
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S11        20   AU="HEATH, ANDREW W."
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              27  S10
               0  S20
     S12       0  S9 AND S10 AND S20
? rd s9,s10,s20
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? rd s9

>>>Duplicate detection is not supported for File 351.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
     S13       46  RD S9 (unique items)
? rd s10

>>>Duplicate detection is not supported for File 351.

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     S14       27  RD S10 (unique items)
? rd s20

>>>Set 20 has not yet been created.
? rd s11

>>>Duplicate detection is not supported for File 351.

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? s s13 and s14 and s15

               46  S13
               27  S14
               20  S15
     S16        0  S13 AND S14 AND S15
? t s13/3/all


 13/3/1      (Item 1 from file: 55)
DIALOG(R)File  55:BIOSIS PREVIEWS(R)
(c) 1998 BIOSIS. All rts. reserv.

14145430      BIOSIS Number: 01145430
  The influence of vaccine formulation on cytokine levels and subclass
antibody responses of HSV-2 immunised mice
  Mohamedi S A; Heath A W; Jennings R
  Dep. Med. Microbiol., Univ. Sheffield Med. Sch., Beech Hill Road,
Sheffield S10 2EX, UK
  Journal of Medical Microbiology 46 (12). 1997.  1053.
  Full Journal Title:  175th Meeting of the Pathological Society of Great
Britain and Ireland, Sheffield, England, UK, July 2-4, 1997.  Journal of
Medical Microbiology
  ISSN: 0022-2615
  Language: ENGLISH
  Document Type: CONFERENCE PAPER
  Print Number: Biological Abstracts/RRM Vol. 050 Iss. 004 Ref. 053314


 13/3/2      (Item 2 from file: 55)
DIALOG(R)File  55:BIOSIS PREVIEWS(R)
(c) 1998 BIOSIS. All rts. reserv.

14107180      BIOSIS Number: 01107180
  Development of a novel cytokine-antigen fusion protein to enhance the
immune response to recombinant gp120 of HIV-1
  McCormick A L; Thomas M S; Heath A W
  Dep. Med. Microbiol., Univ. Sheffield Med. Sch., Beech Hill Road,
Sheffield S10 2RX, UK
```

Immunology 92 (SUPPL. 1). 1997. 57.
Full Journal Title: 5th Annual Congress of the British Society for Immunology, Brighton, England, UK, December 2-5, 1997. Immunology
ISSN: 0019-2805
Language: ENGLISH
Document Type: CONFERENCE PAPER
Print Number: Biological Abstracts/RRM Vol. 050 Iss. 003 Ref. 041092

13/3/3 (Item 3 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

14107118 BIOSIS Number: 01107118
Suppression of alloantibody responses by CD40 ligand expression
McCormick A L; Thomas M S; **Heath A W**
Dep. Medical Microbiol., Univ. Sheffield Medical Sch., Beech Hill Rd., Sheffield S10 2RX, UK
Immunology 92 (SUPPL. 1). 1997. 45.
Full Journal Title: 5th Annual Congress of the British Society for Immunology, Brighton, England, UK, December 2-5, 1997. Immunology
ISSN: 0019-2805
Language: ENGLISH
Document Type: CONFERENCE PAPER
Print Number: Biological Abstracts/RRM Vol. 050 Iss. 003 Ref. 041030

13/3/4 (Item 4 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

14078930 BIOSIS Number: 01078930
Enhancement of T cell-independent immune responses in vivo by CD40 antibodies
Dullforce P; Sutton D C; **Heath A W**
Div. Molecular Genetic Med., Univ. Sheffield Med. Sch., Beech Hill Road, Sheffield S10 2RX, UK
Nature Medicine 4 (1). 1998. 88-91.
Full Journal Title: Nature Medicine
ISSN: 1078-8956
Language: ENGLISH
Print Number: Biological Abstracts Vol. 105 Iss. 004 Ref. 051205

13/3/5 (Item 5 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

13631535 BIOSIS Number: 99631535
Enhancement of immunogenicity of recombinant antigens by production of a cytokine-antigen fusion protein for vaccination
McCormick A L; Thomas M S; **Heath A W**
Dep. Med. Microbiology, Univ. Sheffield Med. Sch., Sheffield S10 2RX, UK
Biochemical Society Transactions 25 (2). 1997. 297S.
Full Journal Title: 660th Meeting of the Biochemical Society, Joint Congress with the British Society for Immunology, Harrogate, England, UK, December 10-13, 1996. Biochemical Society Transactions
ISSN: 0300-5127
Language: ENGLISH
Document Type: CONFERENCE PAPER
Print Number: Biological Abstracts/RRM Vol. 049 Iss. 008 Ref. 138100

13/3/6 (Item 6 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

13631510 BIOSIS Number: 99631510
Large scale comparison of adjuvant effects on immunogenicity and protection in a Herpes Simplex Virus type 1 vaccination model
Simms J R; **Heath A W**; Richardson V J; Jennings R
Dep. Med. Microbiol., Univ. Sheffield Med. Sch., Sheffield S10 2RX, UK
Biochemical Society Transactions 25 (2). 1997. 272S.
Full Journal Title: 660th Meeting of the Biochemical Society, Joint Congress with the British Society for Immunology, Harrogate, England, UK, December 10-13, 1996. Biochemical Society Transactions
ISSN: 0300-5127
Language: ENGLISH
Document Type: CONFERENCE PAPER
Print Number: Biological Abstracts/RRM Vol. 049 Iss. 008 Ref. 138075

13/3/7 (Item 7 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

13402147 BIOSIS Number: 99402147
Large scale comparison of adjuvant effects on immunogenicity and protection in an HSV-1 vaccination model
Simms J R; **Heath A W**; Richardson V J; Jennings R
Dep. Med. Microbiol., Univ. Sheffield Med. Sch., Sheffield S10 2RX, UK
Immunology 89 (SUPPL. 1). 1996. 64.
Full Journal Title: Joint Congress of the British Society for Immunology and the Biochemical Society, Harrogate, England, UK, December 10-13, 1996. Immunology
ISSN: 0019-2805
Language: ENGLISH
Document Type: CONFERENCE PAPER
Print Number: Biological Abstracts/RRM Vol. 049 Iss. 003 Ref. 048786

13/3/8 (Item 8 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

13335622 BIOSIS Number: 99335622
CD40 signaling induces interleukin-4-independent IgE switching in vivo
Ferlin W G; Severinson E; Stroem L; **Heath A W**; Coffman R L; Ferrick D A; Howard M C
DNAX Res. Inst., 901 California Ave., Palo Alto, CA 94304-1104, USA
European Journal of Immunology 26 (12). 1996. 2911-2915.
Full Journal Title: European Journal of Immunology
ISSN: 0014-2980
Language: ENGLISH
Print Number: Biological Abstracts Vol. 103 Iss. 003 Ref. 038736

13/3/9 (Item 9 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

13247670 BIOSIS Number: 99247670
Differential effects of transforming growth factor-beta-1 on IgA vs IgG2b production by lipopolysaccharide-stimulated lymph node B cells: A comparative study with spleen B cells
Garcia B; Rodriguez R; Angulo I; **Heath A W**; Howard M C; Subiza J L
Dep. Immunol., Hosp. Univ. San Carlos, E-28040 Madrid, Spain
European Journal of Immunology 26 (10). 1996. 2364-2370.
Full Journal Title: European Journal of Immunology
ISSN: 0014-2980

Language: ENGLISH
Print Number: Biological Abstracts Vol. 102 Iss. 011 Ref. 163300

13/3/10 (Item 10 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

13066530 BIOSIS Number: 99066530
Cytokines as immunological adjuvants
Heath A W
Dep. Med. Microbiol., Univ. Sheffield Med. Sch., Sheffield S10 2RX, UK
0 (0). 1995. 645-658.
Full Journal Title: Powell, M. F. and M. J. Newman (Ed.). Pharmaceutical Biotechnology, Vol. 6. Vaccine design: The subunit and adjuvant approach. xlv+949p. Plenum Press: New York, New York, USA; London, England, UK. ISBN 0-306-44867-X.
ISSN: *********
Language: ENGLISH
Document Type: BOOK
Print Number: Biological Abstracts/RRM Vol. 048 Iss. 008 Ref. 131710

13/3/11 (Item 11 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11796474 BIOSIS Number: 98396474
CD40 function as defined by the in vivo administration of anti-CD40 mAb
Ferlin W G; **Heath A W**; Howard M
DNAX Res. Inst. Palo Alto, CA, USA
0 (0). 1995. 264.
Full Journal Title: 9TH INTERNATIONAL CONGRESS OF IMMUNOLOGY. The 9th International Congress of Immunology; Meeting Sponsored by the American Association of Immunologists and the International Union of Immunological Societies, San Francisco, California, USA, July 23-29, 1995. ix+742p. 9th International Congress of Immunology: San Francisco, California, USA.
ISSN: *********
Language: ENGLISH
Document Type: CONFERENCE PAPER
Print Number: Biological Abstracts/RRM Vol. 047 Iss. 009 Ref. 158877

13/3/12 (Item 12 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11760141 BIOSIS Number: 98360141
Signaling through murine CD38 is impaired in antigen receptor-unresponsive B cells
Lund F E; Solvason N W; Cooke M P; **Heath A W**; Grimaldi J C; Parkhouse R M E; Goodnow C C; Howard M C
DNAX Res. Inst., 901 California Ave., Palo Alto, CA 94304, USA
European Journal of Immunology 25 (5). 1995. 1338-1345.
Full Journal Title: European Journal of Immunology
ISSN: 0014-2980
Language: ENGLISH
Print Number: Biological Abstracts Vol. 100 Iss. 004 Ref. 051979

13/3/13 (Item 13 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11640454 BIOSIS Number: 98240454

Cytokines as adjuvants in immunocompromised hosts
Heath A W
Dep. Medical Microbiol., Univ. Sheffield Medical Sch., Beech Hill Road, Sheffield S10 2R, UK
International Journal of Clinical & Laboratory Research 25 (1). 1995. 25-28.
Full Journal Title: International Journal of Clinical & Laboratory Research
ISSN: 0940-5437
Language: ENGLISH
Print Number: Biological Abstracts Vol. 099 Iss. 011 Ref. 162630

13/3/14 (Item 14 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11571257 BIOSIS Number: 98171257
CD38 unresponsiveness of xid B cells implicates Bruton's tyrosine kinase (btk) as a regulator of CD38 induced signal transduction
Santos-Argumedo L; Lund F E; **Heath A W**; Solvason N; Wu W W; Grimaldi J C; Parkhouse R M E; Howard M
DNAX Research Inst., 901 California Ave., Palo Alto, CA 94304, USA
International Immunology 7 (2). 1995. 163-170.
Full Journal Title: International Immunology
ISSN: 0953-8178
Language: ENGLISH
Print Number: Biological Abstracts Vol. 099 Iss. 008 Ref. 111560

13/3/15 (Item 15 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11244583 BIOSIS Number: 97444583
Monoclonal antibodies to murine CD40 define two distinct functional epitopes
Heath A W; Wu W W; Howard M C
DNAX Res. Inst., 901 California Ave., Palo Alto, CA 94304, USA
European Journal of Immunology 24 (8). 1994. 1828-1834.
Full Journal Title: European Journal of Immunology
ISSN: 0014-2980
Language: ENGLISH
Print Number: Biological Abstracts Vol. 098 Iss. 008 Ref. 098895

13/3/16 (Item 16 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11204497 BIOSIS Number: 97404497
Antibodies to murine CD40 protection normal and malignant B cells from induced growth arrest
Santos-Argumedo L; Gordon J; **Heath A W**; Howard M
DNAX Res. Inst., 901 California Ave., Palo Alto, CA 94304, USA
Cellular Immunology 156 (2). 1994. 272-285.
Full Journal Title: Cellular Immunology
ISSN: 0008-8749
Language: ENGLISH
Print Number: Biological Abstracts Vol. 098 Iss. 006 Ref. 075309

13/3/17 (Item 17 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11139457 BIOSIS Number: 97339457
Immunoglobulin signal transduction guides B cell-T cell interactions and is blocked in tolerant self-reactive B cells
Cooke M P; **Heath A W**; Shokat K M; Zeng Y; Howard M; Goodnow C C
Howard Hughes Med. Inst., Stanford Univ., Stanford, CA 94305, USA
Journal of Cellular Biochemistry Supplement 0 (18D). 1994. 397.
Full Journal Title: Keystone Symposium on Lymphocyte Activation, Keystone, Colorado, USA, April 10-17, 1994. Journal of Cellular Biochemistry Supplement
ISSN: 0733-1959
Language: ENGLISH
Document Type: CONFERENCE PAPER
Print Number: Biological Abstracts/RRM Vol. 046 Iss. 008 Ref. 117175

13/3/18 (Item 18 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11139366 BIOSIS Number: 97339366
CD40 and murine B cell ontogeny
Heath A W; Wu W W; Cyster J G; Goodnow C C; Howard M
DNAX Res. Inst., Palo Alto, CA, USA
Journal of Cellular Biochemistry Supplement 0 (18D). 1994. 373.
Full Journal Title: Keystone Symposium on Lymphocyte Activation, Keystone, Colorado, USA, April 10-17, 1994. Journal of Cellular Biochemistry Supplement
ISSN: 0733-1959
Language: ENGLISH
Document Type: CONFERENCE PAPER
Print Number: Biological Abstracts/RRM Vol. 046 Iss. 008 Ref. 117084

13/3/19 (Item 19 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11085065 BIOSIS Number: 97285065
Vaccination against the cat flea Ctenocephalides felis felis
Heath A W; Arfsten A; Yamanaka M; Dryden M W; Dale B
Dep. Immunol., DNAX Res. Inst., 901 California Ave., Palo Alto, CA 94304, USA
Parasite Immunology (Oxford) 16 (4). 1994. 187-191.
Full Journal Title: Parasite Immunology (Oxford)
ISSN: 0141-9838
Language: ENGLISH
Print Number: Biological Abstracts Vol. 098 Iss. 001 Ref. 006710

13/3/20 (Item 20 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11072506 BIOSIS Number: 97272506
Cytokines and the rational choice of immunological adjuvants
Heath A W
DNAX Res. Inst., 901 California Ave., Palo Alto, CA 94025, USA
Cancer Biotherapy 9 (1). 1994. 1-6.
Full Journal Title: Cancer Biotherapy
ISSN: 1062-8401
Language: ENGLISH
Print Number: Biological Abstracts Vol. 097 Iss. 012 Ref. 174056

13/3/21 (Item 21 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
(c) 1998 BIOSIS. All rts. reserv.

10940600 BIOSIS Number: 97140600
Immunoglobulin signal transduction guides the specificity of B cell-T cell interactions and is blocked in tolerant self-reactive B cells
Cooke M P; **Heath A W**; Shokat K M; Zeng Y; Finkelman F D; Linsley P S; Howard M; Goodnow C C
Howard Hughes Med. Inst. Res. Lab., Beckman Cent. Mol. Genet. Med., Stanford Univ. Med. Cent., Stanford, CA 94305-5428, USA
Journal of Experimental Medicine 179 (2). 1994. 425-438.
Full Journal Title: Journal of Experimental Medicine
ISSN: 0022-1007
Language: ENGLISH
Print Number: Biological Abstracts Vol. 097 Iss. 007 Ref. 090482

13/3/22 (Item 22 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
(c) 1998 BIOSIS. All rts. reserv.

10926011 BIOSIS Number: 97126011
Antibodies to murine CD40 stimulate normal B lymphocytes but inhibit proliferation of B lymphoma cells
Heath A W; Chang R; Harada N; Santos-Argumedo L; Gordon J; Hannum C ; Campbell D; Shanafelt A B; Clark E A; et al
Inq.: Maureen Howard, DNAX Research Inst., 901 California Ave., Palo Alto, CA 94304, USA
Cellular Immunology 152 (2). 1993. 468-480.
Full Journal Title: Cellular Immunology
ISSN: 0008-8749
Language: ENGLISH
Print Number: Biological Abstracts Vol. 097 Iss. 006 Ref. 075886

13/3/23 (Item 23 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
(c) 1998 BIOSIS. All rts. reserv.

10805374 BIOSIS Number: 97005374
Expression of the murine interleukin-4 gene in an attenuated aroA strain of Salmonella typhimurium: Persistence and immune response in BALB-c mice and susceptibility to macrophage killing
Denich K; Borlin P; O'Hanley P D; Howard M; **Heath A W**
Dep. Med., Div. Infectious Diseases Geographic Med., Stanford Univ., Stanford, CA 94305-5402, USA
Infection and Immunity 61 (11). 1993. 4818-4827.
Full Journal Title: Infection and Immunity
ISSN: 0019-9567
Language: ENGLISH
Print Number: Biological Abstracts Vol. 097 Iss. 001 Ref. 004908

13/3/24 (Item 24 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
(c) 1998 BIOSIS. All rts. reserv.

10536002 BIOSIS Number: 96136002
EXPRESSION CLONING OF A CDNA ENCODING A NOVEL MURINE B CELL ACTIVATION MARKER HOMOLOGY TO HUMAN CD38
HARADA N; SANTOS-ARGUMEDO L; CHANG R; GRIMALDI J C; LUND F E; BRANNAN C I ; COPELAND N G; JENKINS N A; **HEATH A W**; ET AL
INQ.: MAUREEN HOWARD, DNAX RES. INST., 901 CALIFORNIA AVE., PALO ALTO, CA 94304, USA.

J IMMUNOL 151 (6). 1993. 3111-3118. CODEN: JOIMA
Full Journal Title: Journal of Immunology
Language: ENGLISH

13/3/25 (Item 25 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

9864705 BIOSIS Number: 44114705
CLONING OF A NOVEL B CELL ACTIVATION ANTIGEN RELATED TO HUMAN CD38
SANTOS-ARGUMEDO N H; CHANG R; **HEATH A W**; GRIMALDI C; PARKHOUSE R M E; HOWARD M
DNAX RES. INST., PALO ALTO, CA, USA.
KEYSTONE SYMPOSIUM ON B CELL IMMUNOBIOLOGY AND HUMAN DISEASE, TAOS, NEW MEXICO, USA, FEBRUARY 1-8, 1993. J CELL BIOCHEM SUPPL 0 (17 PART B). 1993. 169. CODEN: JCBSD
Language: ENGLISH
Document Type: CONFERENCE PAPER

13/3/26 (Item 26 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

9770602 BIOSIS Number: 44020602
THE POTENTIAL OF CYTOKINES AS ADJUVANTS
HEATH A W; PLAYFAIR J H L
DNAX RES. INST., 901 CALIF. AVE., PALO ALTO, CALIF. 94304.
INTERNATIONAL CONFERENCE ON ADVANCES IN AIDS VACCINE DEVELOPMENT AND THE FOURTH ANNUAL MEETING OF THE NATIONAL COOPERATIVE VACCINE DEVELOPMENT GROUP FOR AIDS, MARCO ISLAND, FLORIDA, USA, OCTOBER 15-19, 1991. AIDS RES HUM RETROVIRUSES 8 (8). 1992. 1401-1403. CODEN: ARHRE
Language: ENGLISH
Document Type: CONFERENCE PAPER

13/3/27 (Item 27 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

9364778 BIOSIS Number: 43109778
INTERFERON-GAMMA AS AN ADJUVANT FOR VACCINES
HEATH A W; PLAYFAIR J H L
DNAX RES. INST. MOL. AND CELL. BIOL., PALO ALTO, CALIF.
JAFFE, H. S., L. R. BUCALO AND S. A. SHERWIN (ED.). ANTI-INFECTIVE APPLICATIONS OF INTERFERON-GAMMA. XIII+316P. MARCEL DEKKER, INC.: NEW YORK, NEW YORK, USA; BASEL, SWITZERLAND. ILLUS. ISBN 0-8247-8688-2. 0 (0). 1992. 295-307. CODEN: 43242
Language: ENGLISH

13/3/28 (Item 28 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

8552300 BIOSIS Number: 92017300
MONOCLONAL ANTIBODIES MEDIATING VIABLE IMMUNOFLUORESCENCE AND PROTECTION AGAINST TRYPANOSOMA-CRUZI INFECTION
HEATH A W; MARTINS M S; HUDSON L
DIV. CELLULAR MOL. SCI., GLAXO GROUP RES. LTD., GREENFORD, MIDDLESEX UB6 OHE, UK.
TROP MED PARASITOL 41 (4). 1990. 425-428. CODEN: TMPAE
Language: ENGLISH

13/3/29 (Item 29 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

8539947 BIOSIS Number: 92004947
EFFECTS OF INTERFERON GAMMA AND SAPONIN ON LYMPHOCYTE TRAFFIC ARE INVERSELY RELATED TO ADJUVANTICITY AND ENHANCEMENT OF MHC CLASS II EXPRESSION
HEATH A W; NYAN O; RICHARDS C E; PLAYFAIR J H L
PARAVAX INC., 2462 WYANDOTTE ST., MOUNTAIN VIEW, CALIF. 94043, USA.
INT IMMUNOL 3 (3). 1991. 285-292. CODEN: INIME
Language: ENGLISH

13/3/30 (Item 30 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

8319077 BIOSIS Number: 41003077
PROBLEM-FOCUSED SUPERVISION RATIONALE EXEMPLIFICATION AND LIMITATIONS
STORM C L; **HEATH A W**
PACIFIC LUTHERAN UNIV., TACOMA, WASH.
J FAM PSYCHOTHER 2 (1). 1991. 55-70. CODEN: JFAPE
Language: ENGLISH

13/3/31 (Item 31 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

8110406 BIOSIS Number: 91031406
CONJUGATION OF INTERFERON-GAMMA TO ANTIGEN ENHANCES ITS ADJUVANTICITY
HEATH A W; PLAYFAIR J H L
PAROVAX INC., 2462 WYANDOTE ST., MOUNTAIN VIEW, CALIF. 94043, USA.
IMMUNOLOGY 71 (3). 1990. 454-456. CODEN: IMMUA
Full Journal Title: Immunology
Language: ENGLISH

13/3/32 (Item 32 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

7876862 BIOSIS Number: 40077862
FAMILY THERAPY
HEATH A W; STANTON M D
DEP. HUM. FAM. RESOURCES, NORTH. ILL. UNIV., DEKALB, ILL., USA.
FRANCES, R. J. AND S. I. MILLER (ED.). THE GUILFORD SUBSTANCE ABUSE SERIES: CLINICAL TEXTBOOK OF ADDICTIVE DISORDERS. XIX+540P. GUILFORD PRESS: NEW YORK, NEW YORK, USA; LONDON, ENGLAND, UK. ILLUS. ISBN 0-89862-552-1. 0 (0). 1991. 406-430. CODEN: 32637
Language: ENGLISH
Document Type: CONFERENCE PAPER

13/3/33 (Item 33 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

7534133 BIOSIS Number: 39046740
CYTOKINES AND INFECTION
HEATH A W
DEP. IMMUNOL., UNIV. COLL. MIDDLESEX SCH. MED., LONDON, UK.
CURR OPIN IMMUNOL 2 (3). 1990. 380-384. CODEN: COPIE

Language: ENGLISH

13/3/34 (Item 34 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

7174134 BIOSIS Number: 88096879
INTERFERON-GAMMA AS AN ADJUVANT IN IMMUNOCOMPROMISED MICE
HEATH A W; DEVEY M E; BROWN I N; RICHARDS C E; PLAYFAIR J H L
DEP. IMMUNOL., UNIV. COLL. MIDDLESEX SCH. MED., ARTHUR STANLEY HOUSE, 40-50 TOTTENHAM ST., LONDON W1P 9PG, UK.
IMMUNOLOGY 67 (4). 1989. 520-524. CODEN: IMMUA
Full Journal Title: Immunology
Language: ENGLISH

13/3/35 (Item 35 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

5747519 BIOSIS Number: 83009826
COLD ADAPTED REASSORTANTS OF INFLUENZA A VIRUS PATHOGENICITY OF A-ANN-ARBOR-6-60 X A-ALASKA-6-77 REASSORTANT VIRUSES IN-VIVO AND IN-VITRO
HEATH A W; MAASSAB H F; ODAGIRI T; DEBORDE D C; POTTER C W
DEP. IMMUNOL., ST. GEORGES HOSP. MED. SCH., CRANMER TERRACE, LONDON SW17 0RE, U.K.
ARCH VIROL 91 (1-2). 1986. 53-60. CODEN: ARVID
Full Journal Title: Archives of Virology
Language: ENGLISH

13/3/36 (Item 1 from file: 351)
DIALOG(R)File 351:DERWENT WPI

011549723 **Image available**
WPI Acc No: 97-526204/199748
XRAM Acc No: C97-167360
Vaccine for enhancing T cell response containing antigen and adjuvant acting via the CD28 receptor - also the new adjuvants and DNA encoding them or T cell dependent antigens
Patent Assignee: UNIV SHEFFIELD (UYSH-N)
Inventor: **HEATH A W**
Number of Countries: 076 Number of Patents: 003
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
WO 9738711	A2	19971023	WO 97GB971	A	19970408	A61K-039/00	199748 B
AU 9723031	A	19971107	AU 9723031	A	19970408	A61K-039/00	199809
WO 9738711	A3	19971120	WO 97GB971	A	19970408	A61K-039/00	199816

Priority Applications (No Type Date): GB 967711 A 19960413
Filing Details:

Patent	Kind	Filing Notes	Application	Patent
WO 9738711	A2			
		Designated States (National): AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU		
		Designated States (Regional): AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG		
AU 9723031	A	Based on	WO 9738711	

Language, Pages: WO 9738711 (E, 31)

13/3/37 (Item 2 from file: 351)
DIALOG(R)File 351:DERWENT WPI

009803260
WPI Acc No: 94-083114/199410
XRAM Acc No: C94-038078
New soluble form of CD40 and B cell CD40 ligand - for inhibiting growth of CD40 positive malignant, esp B lymphoma, cells or reducing T cell activity against CD40 positive cells
Patent Assignee: SCHERING CORP (SCHE)
Inventor: **HEATH A W**; HOWARD M; LANIER L L
Number of Countries: 043 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
WO 9404570	A1	19940303	WO 93US7673	A	19930819	C07K-015/06	199410 B
AU 9350984	A	19940315	AU 9350984	A	19930819	C07K-015/06	199428

Priority Applications (No Type Date): US 92934371 A 19920821
Filing Details:

Patent	Kind	Filing Notes	Application	Patent
WO 9404570	A1			
		Designated States (National): AU BB BG BR BY CA CZ FI HU JP KR KZ LK MG MN MW NO NZ PL RO RU SD SK UA US VN		
		Designated States (Regional): AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE		
AU 9350984	A	Based on		WO 9404570

Language, Pages: WO 9404570 (E, 46)

13/3/38 (Item 3 from file: 351)
DIALOG(R)File 351:DERWENT WPI

009520281
WPI Acc No: 93-213823/199326
Related WPI Acc No: 96-221762
XRAM Acc No: C93-094826
Vaccine for protecting avian(s) and mammals against flea infestation - comprises supernatant fraction of flea mid-gut, useful in purification, diagnosis and passive therapy
Patent Assignee: PARAVAX INC (PARA-N)
Inventor: ARFSTEN A; DALE B; **HEATH A W**; YAMANAKA M
Number of Countries: 020 Number of Patents: 003
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
WO 9311790	A1	19930624	WO 92US10671	A	19921210	A61K-039/00	199326 B
AU 9332470	A	19930719	AU 9332470	A	19921210	A61K-039/00	199344
US 5356622	A	19941018	US 91806482	A	19911213	A61K-039/35	199441

Priority Applications (No Type Date): US 91806482 A 19911213
Filing Details:

Patent	Kind	Filing Notes	Application	Patent
WO 9311790	A1			
		Designated States (National): AU JP NZ		
		Designated States (Regional): AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE		
AU 9332470	A	Based on		WO 9311790

Language, Pages: WO 9311790 (E, 35); US 5356622 (14)

13/3/39 (Item 4 from file: 351)
DIALOG(R)File 351:DERWENT WPI

008969327
WPI Acc No: 92-096596/199212
XRAM Acc No: C92-044814
Vaccine compsn. for protection against flea infestation - comprises membranes or membrane extracts of fleas, esp. derived from flea mid-guts
Patent Assignee: PARAVAX INC (PARA-N); UNIV QUEENSLAND (UYQU)
Inventor: ARFSTEN A E; BOREHAM R E; DALE B; **HEATH A W**; OPDEBEECK J P; STEVENSON L B; YAMANAKE M K; BOR
Number of Countries: 013 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
WO 9203156	A	19920305	WO 91US5852	A	19910815		199212 B
AU 9185370	A	19920317	AU 9185370	A	19910815	A61K-039/00	199226
			WO 91US5852	A	19910815		

Priority Applications (No Type Date): US 90571257 A 19900822
Filing Details:

Patent	Kind	Filing Notes	Application	Patent
WO 9203156	A			
		Designated States (National): AU CA JP		
		Designated States (Regional): AT CH DE DK ES GB GR LU NL SE		
AU 9185370	A	Based on		WO 9203156

Language, Pages: WO 9203156 (30)

13/3/40 (Item 5 from file: 351)
DIALOG(R)File 351:DERWENT WPI

007417203 **Image available**
WPI Acc No: 88-051138/198808
XRPX Acc No: N88-038838
Data processing system for input device interface - has program enabling capture of keystrokes and uses mouse to point to table of zones stored relative to each menu for computer
Patent Assignee: INT BUSINESS MACHINES CORP (IBMC); IBM CORP (IBMC)
Inventor: BULLOCK G R; **HEATH A W**; SHEPPARD R K
Number of Countries: 005 Number of Patents: 005
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
EP 256220	A	19880224	EP 87106901	A	19870512		198808 B
BR 8702796	A	19880301					198814
US 4755808	A	19880705	US 86873758	A	19860613		198829
EP 256220	B1	19921230	EP 87106901	A	19870512	G06K-011/06	199301
DE 3783286	G	19930211	DE 3783286	A	19870512	G06K-011/06	199307
			EP 87106901	A	19870512		

Priority Applications (No Type Date): US 86873758 A 19860613
Filing Details:

Patent	Kind	Filing Notes	Application	Patent
EP 256220	A			
		Designated States (Regional): DE FR GB		
EP 256220	B1			
		Designated States (Regional): DE FR GB		
DE 3783286	G	Based on		EP 256220

Language, Pages: EP 256220 (E, 19); US 4755808 (14); EP 256220 (E, 21)

13/3/41 (Item 6 from file: 351)
DIALOG(R)File 351:DERWENT WPI

007353117
WPI Acc No: 87-350123/198750
XRPX Acc No: N87-262471

Multi-page document printing system with selectable page ordering - supplies page representation to selected output printer so that pages of document have predetermined orientation
Patent Assignee: IBM CORP (IBMC)
Inventor: **HEATH A W**; LEVINE F E; PAVITZ W L
Number of Countries: 012 Number of Patents: 003
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
EP 249495	A	19871216	EP 87305232	A	19870612		198750 B
AU 8773700	A	19871217					198806
BR 8702848	A	19880301					198814

Priority Applications (No Type Date): US 86873760 A 19860613
Filing Details:

Patent	Kind	Filing Notes	Application	Patent
EP 249495	A			

Designated States (Regional): BE CH DE ES FR GB IT LI NL SE
Language, Pages: EP 249495 (E, 12)

13/3/42 (Item 7 from file: 351)
DIALOG(R)File 351:DERWENT WPI

007352794
WPI Acc No: 87-349800/198750
XRPX Acc No: N87-262240
Data display system with processing unit - uses both keyboard controlled cursor and pointer, e.g. mouse, controlled by pointing device
Patent Assignee: IBM CORP (IBMC)
Inventor: **HEATH A W**; SHEPPARD R K
Number of Countries: 005 Number of Patents: 003
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
EP 249063	A	19871216	EP 87107235	A	19870519		198750 B
BR 8702791	A	19880301					198814
US 4760386	A	19880726	US 86873757	A	19860613		198832

Priority Applications (No Type Date): US 86873757 A 19860613
Filing Details:

Patent	Kind	Filing Notes	Application	Patent
EP 249063	A			

Designated States (Regional): DE FR GB
Language, Pages: EP 249063 (E, 19); US 4760386 (13)

13/3/43 (Item 8 from file: 351)
DIALOG(R)File 351:DERWENT WPI

007023079
WPI Acc No: 87-023076/198704
XRPX Acc No: N87-017477
Compatibility maintenance for different I-O types - performing search upon initial loading of program to determine existence of set of exception tables
Patent Assignee: INT BUSINESS MACHINES CORP (IBMC); IBM CORP (IBMC)
Inventor: **HEATH A W**; HERNANDEZ R; HOFFMANN V M; SHEPPARD R K; STRATTON S D; HERNANDEEZ R
Number of Countries: 006 Number of Patents: 005
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
EP 209693	A	19870128	EP 86107742	A	19860606		198704 B
CA 1258714	A	19890822					198937
US 4858114	A	19890815	US 87132719	A	19871211		198941

EP 209693	B1	19930324	EP 86107742	A	19860606	G06F-009/44		199312
DE 3688107	G	19930429	DE 3688107	A	19860606	G06F-009/44		199318
			EP 86107742	A	19860606			

Priority Applications (No Type Date): US 85757233 A 19850722
Filing Details:

Patent	Kind	Filing Notes	Application	Patent
EP 209693	A			
		Designated States (Regional): DE FR GB IT		
EP 209693	B1			
		Designated States (Regional): DE FR GB IT		
DE 3688107	G	Based on	EP 209693	

Language, Pages: EP 209693 (E, 10); US 4858114 (9); EP 209693 (E, 11)

13/3/44 (Item 9 from file: 351)
DIALOG(R)File 351:DERWENT WPI

004635227
WPI Acc No: 86-138570/198622
XRPX Acc No: N86-102396
Word processing interacting printer format program - enables operator to select one of number of formats for printing super-script and sub-script text
Patent Assignee: INT BUSINESS MACHINES CORP (IBMC); IBM CORP (IBMC)
Inventor: BERKLAND P T; **HEATH A W**; WADDELL G K
Number of Countries: 006 Number of Patents: 005
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
EP 182042	A	19860528	EP 85112094	A	19850924		198622 B
US 4648047	A	19870303	US 84664180	A	19841024		198711
CA 1223966	A	19870707					198731
EP 182042	B1	19930217	EP 85112094	A	19850924	G06F-003/12	199307
DE 3587105	G	19930325	DE 3587105	A	19850924	G06F-003/12	199313
			EP 85112094	A	19850924		

Priority Applications (No Type Date): US 84664180 A 19841024
Filing Details:

Patent	Kind	Filing Notes	Application	Patent
EP 182042	A			
		Designated States (Regional): DE FR GB IT		
EP 182042	B1			
		Designated States (Regional): DE FR GB IT		
DE 3587105	G	Based on	EP 182042	

Language, Pages: EP 182042 (E, 13); EP 182042 (E, 23)

13/3/45 (Item 10 from file: 351)
DIALOG(R)File 351:DERWENT WPI

004610942
WPI Acc No: 86-114286/198618
XRPX Acc No: N86-084176
Controlling placement of document image on paper - by adjusting one edge of image in accordance with entered print position parameter, for processing system with two output printers
Patent Assignee: INT BUSINESS MACHINES CORP (IBMC); IBM CORP (IBMC)
Inventor: BERKLAND P T; **HEATH A W**; WADDELL G K
Number of Countries: 004 Number of Patents: 004
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
EP 179279	A	19860430	EP 85111904	A	19850920		198618 B
US 4656602	A	19870407	US 84664178	A	19841024		198716

EP 179279 B1 19920708 EP 85111904 A 19850920 G06K-015/16 199228
DE 3586308 G 19920813 DE 3586308 A 19850920 G06K-015/16 199234
EP 85111904 A 19850920

Priority Applications (No Type Date): US 84664178 A 19841024
Filing Details:
Patent Kind Filing Notes Application Patent
EP 179279 A
Designated States (Regional): DE FR GB
EP 179279 B1
Designated States (Regional): DE FR GB
DE 3586308 G Based on EP 179279
Language, Pages: EP 179279 (E, 35); EP 179279 (E, 26)

13/3/46 (Item 11 from file: 351)
DIALOG(R)File 351:DERWENT WPI

004610899
WPI Acc No: 86-114243/198618
XRPX Acc No: N86-084142
Printable data stream formatter - uses general print command shells with parameters that are calculated with indexed table
Patent Assignee: INT BUSINESS MACHINES CORP (IBMC); IBM CORP (IBMC)
Inventor: **HEATH A W**
Number of Countries: 005 Number of Patents: 004
Patent Family:
Patent No Kind Date Applicat No Kind Date Main IPC Week
EP 179206 A 19860430 EP 85109460 A 19850730 198618 B
US 4710886 A 19871201 US 84664181 A 19841024 198750
EP 179206 B 19920429 EP 85109460 A 19850730 199218
DE 3585940 G 19920604 DE 3585940 A 19850730 G06F-003/12 199224
EP 85109460 A 19850730

Priority Applications (No Type Date): US 84664181 A 19841024
Filing Details:
Patent Kind Filing Notes Application Patent
EP 179206 A
Designated States (Regional): DE FR GB IT
EP 179206 B
Designated States (Regional): DE FR GB IT
DE 3585940 G Based on EP 179206
Language, Pages: EP 179206 (E, 33); EP 179206 (E, 21)
? t s14/3/all

14/3/1 (Item 1 from file: 72)
DIALOG(R)File 72:EMBASE

10660293 EMBASE No: 98096096
Enhancement of T cell-independent immune responses in vivo by CD40 antibodies
Dullforce P.; Sutton D.C.; **Heath A.W.**
A.W. Heath, Div. of Molec. and Genetic Medicine, Sheffield Inst. for Vaccine Studies, Univ. of Sheffield Medical School, Beech Hill Road, Sheffield S10 2RX United Kingdom
Nature Medicine (United States) , 1998, 4/1 (88-91)
CODEN: NAMEF ISSN: 1078-8956
DOCUMENT TYPE: Journal Article
LANGUAGES: ENGLISH SUMMARY LANGUAGES: ENGLISH
NUMBER OF REFERENCES: 29

14/3/2 (Item 2 from file: 72)
DIALOG(R)File 72:EMBASE

10374189 EMBASE No: 97185639
Enhancement of immunogenicity of recombinant antigens by production of a cytokine-antigen fusion protein for vaccination
McCormick A.L.; Thomas M.S.; **Heath A.W.**
A.L. McCormick, Dept. Medical Microbiology, University of Sheffield, Medical School, Sheffield S10 2RX United Kingdom
Biochemical Society Transactions (United Kingdom) , 1997, 25/2 (297S)
CODEN: BCSTB ISSN: 0300-5127
DOCUMENT TYPE: Journal
LANGUAGES: English
NUMBER OF REFERENCES: 4

14/3/3 (Item 3 from file: 72)
DIALOG(R)File 72:EMBASE

10374164 EMBASE No: 97185614
Large scale comparison of adjuvant effects on immunogenicity and protection in a Herpes Simplex Virus type 1 vaccination model
Simms J.R.; **Heath A.W.**; Richardson V.J.; Jennings R.
J.R. Simms, Dept. Medical Microbiology, University of Sheffield, Medical School, Sheffield S10 2RX United Kingdom
Biochemical Society Transactions (United Kingdom) , 1997, 25/2 (272S)
CODEN: BCSTB ISSN: 0300-5127
DOCUMENT TYPE: Journal
LANGUAGES: English
NUMBER OF REFERENCES: 7

14/3/4 (Item 4 from file: 72)
DIALOG(R)File 72:EMBASE

10186688 EMBASE No: 96372782
CD40 signaling induces interleukin-4-independent IgE switching in vivo
Ferlin W.G.; Severinson E.; Strom L.; **Heath A.W.**; Coffman R.L.; Ferrick D.A.; Howard M.C.
DNAX Research Institute, 901 California Ave, Palo Alto, CA 94304-1104 USA
European Journal of Immunology (Germany) , 1996, 26/12 (2911-2915)
CODEN: EJIMA ISSN: 0014-2980
LANGUAGES: English SUMMARY LANGUAGES: English

14/3/5 (Item 5 from file: 72)
DIALOG(R)File 72:EMBASE

10125220 EMBASE No: 96313461
Differential effects of transforming growth factor-beta1 on IgA vs. IgG2b production by lipapolysaccharide-stimulated lymph node B cells: A comparative study with spleen B cells
Garcia B.; Rodriguez R.; Angulo I.; **Heath A.W.**; Howard M.C.; Subiza J.L.
Department of Immunology, Hosp Univ San Carlos, E-28040 Madrid Spain
European Journal of Immunology (Germany) , 1996, 26/10 (2364-2370)
CODEN: EJIMA ISSN: 0014-2980
LANGUAGES: English SUMMARY LANGUAGES: English

14/3/6 (Item 6 from file: 72)
DIALOG(R)File 72:EMBASE

9799069 EMBASE No: 95330652
The effect of antigen dose on CD4+ T helper cell phenotype development in a T cell receptor-alphabeta-transgenic model
Hosken N.A.; Shibuya K.; **Heath A.W.**; Murphy K.M.; O'Garra A.
DNAX Research Institute, 901 California Avenue, Palo Alto, CA 94304-1104 USA
Journal of Experimental Medicine (USA) , 1995, 182/5 (1579-1584)
CODEN: JEMEA ISSN: 0022-1007
LANGUAGES: English SUMMARY LANGUAGES: English

14/3/7 (Item 7 from file: 72)
DIALOG(R)File 72:EMBASE

9617781 EMBASE No: 95168230
Signaling through murine CD38 is impaired in antigen receptor-unresponsive B cells
Lund F.E.; Solvason N.W.; Cooke M.P.; **Heath A.W.**; Grimaldi J.C.; Parkhouse R.M.E.; Goodnow C.C.; Howard M.C.
DNAX Research Institute, 901 California Ave, Palo Alto, CA 94304 USA
European Journal of Immunology (Germany) , 1995, 25/5 (1338-1345)
CODEN: EJIMA ISSN: 0014-2980
LANGUAGES: English SUMMARY LANGUAGES: English

14/3/8 (Item 8 from file: 72)
DIALOG(R)File 72:EMBASE

9494331 EMBASE No: 95065649
CD38 unresponsiveness of xid B cells implicates Bruton's tyrosine kinase (btk) as a regulator of CD38 induced signal transduction
Santos-Argumedo L.; Lund F.E.; **Heath A.W.**; Solvason N.; Wu W.W.; Grimaldi J.C.; Parkhouse R.M.E.; Howard M.
DNAX Research Institute, 901 California Avenue, Palo Alto, CA 94304 USA
International Immunology (United Kingdom) , 1995, 7/2 (163-170)
CODEN: INIME ISSN: 0953-8178
LANGUAGES: English SUMMARY LANGUAGES: English

14/3/9 (Item 9 from file: 72)
DIALOG(R)File 72:EMBASE

9308751 EMBASE No: 94251867
Antibodies to murine CD40 protect normal and malignant B cells from induced growth arrest
Santos-Argumedo L.; Gordon J.; **Heath A.W.**; Howard M.
DNAX Research Institute, 901 California Avenue, Palo Alto, CA 94304 USA
CELL. IMMUNOL. (USA) , 1994, 156/2 (272-285)
CODEN: CLIMB ISSN: 0008-8749
LANGUAGES: English SUMMARY LANGUAGES: English

14/3/10 (Item 10 from file: 72)
DIALOG(R)File 72:EMBASE

9293182 EMBASE No: 94249570
Monoclonal antibodies to murine CD40 define two distinct functional

epitopes
Heath A.W.; Wu W.W.; Howard M.C.
DNAX Research Institute, 901 California Avenue, Palo Alto, CA 94304 USA
EUR. J. IMMUNOL. (Germany) , 1994, 24/8 (1828-1834)
CODEN: EJIMA ISSN: 0014-2980
LANGUAGES: English SUMMARY LANGUAGES: English

14/3/11 (Item 11 from file: 72)
DIALOG(R)File 72:EMBASE

9235378 EMBASE No: 94178636
Vaccination against the cat flea Ctenocephalides felis felis
Heath A.W.; Arfsten A.; Yamanaka M.; Dryden M.W.; Dale B.
Department of Immunology, DNAX, Research Institute, 901 California Avenue, Palo Alto, CA 94304 USA
PARASITE IMMUNOL. (United Kingdom) , 1994, 16/4 (187-191)
CODEN: PAIMD ISSN: 0141-9838
LANGUAGES: English SUMMARY LANGUAGES: English

14/3/12 (Item 12 from file: 72)
DIALOG(R)File 72:EMBASE

9140056 EMBASE No: 94085510
Cytokines and the rational choice of immunological adjuvants
Heath A.W.
DNAX Research Institute, 901 California Avenue, Palo Alto, CA 94025 USA
CANCER BIOTHER. (USA) , 1994, 9/1 (1-6)
CODEN: CNBTE ISSN: 1062-8401
LANGUAGES: English

14/3/13 (Item 13 from file: 72)
DIALOG(R)File 72:EMBASE

9117642 EMBASE No: 94061226
Immunoglobulin signal transduction guides the specificity of B cell-T cell interactions and is blocked in tolerant self-reactive B cells
Cooke M.P.; **Heath A.W.**; Shokat K.M.; Zeng Y.; Finkelman F.D.; Linsley P.S.; Howard M.; Goodnow C.C.
Beckman Molec./Genetic Medicine Ctr., Howard Hughes Med. Inst. Res. Lab., Stanford University Medical Center, Stanford, CA 94305-5428 USA
J. EXP. MED. (USA) , 1994, 179/2 (425-438)
CODEN: JEMEA ISSN: 0022-1007
LANGUAGES: English SUMMARY LANGUAGES: English

14/3/14 (Item 14 from file: 72)
DIALOG(R)File 72:EMBASE

9099660 EMBASE No: 94032507
Antibodies to murine CD40 stimulate normal B lymphocytes but inhibit proliferation of B lymphoma cells
Heath A.W.; Chang R.; Harada N.; Santos-Argumedo L.; Gordon J.; Hannum C.; Campbell D.; Shanafelt A.B.; Clark E.A.; Torres R.; Howard M.
DNAX Research Institute, 901 California Avenue, Palo Alto, CA 94304 USA
CELL. IMMUNOL. (USA) , 1993, 152/2 (468-480)
CODEN: CLIMB ISSN: 0008-8749
LANGUAGES: English SUMMARY LANGUAGES: English

14/3/15 (Item 15 from file: 72)
DIALOG(R)File 72:EMBASE

9016790 EMBASE No: 93320555
Expression of the murine interleukin-4 gene in an attenuated aroA strain of Salmonella typhimurium: Persistence and immune response in BALB/c mice and susceptibility to macrophage killing
Denich K.; Borlin P.; O'Hanley P.D.; Howard M.; **Heath A.W.**
Infectious Dis./Geographic Med. Div., Department of Medicine, Stanford University, Stanford, CA 94305-5402 USA
INFECT. IMMUN. (USA) , 1993, 61/11 (4818-4827)
CODEN: INFIB ISSN: 0019-9567
LANGUAGES: English SUMMARY LANGUAGES: English

14/3/16 (Item 16 from file: 72)
DIALOG(R)File 72:EMBASE

8978909 EMBASE No: 93282636
Expression cloning of a cDNA encoding a novel murine B cell activation marker: Homology to human CD38
Harada N.; Santos-Argumedo L.; Chang R.; Grimaldi J.C.; Lund F.E.; Brannan C.I.; Copeland N.G.; Jenkins N.A.; **Heath A.W.**; Parkhouse R.M.E.; Howard M.
DNAX Research Institute, 901 California Avenue, Palo Alto, CA 94304 USA
J. IMMUNOL. (USA) , 1993, 151/6 (3111-3118)
CODEN: JOIMA ISSN: 0022-1767
LANGUAGES: English SUMMARY LANGUAGES: English

14/3/17 (Item 17 from file: 72)
DIALOG(R)File 72:EMBASE

8969185 EMBASE No: 93273105
Cytokine-antigen vaccines (7)
Heath A.W.; Playfair J.H.L.
DNAX Research Institute, 901 California Ave, Palo Alto, CA 94303 USA
NATURE (United Kingdom) , 1993, 364/6437 (493)
CODEN: NATUA ISSN: 0028-0836
LANGUAGES: English

14/3/18 (Item 18 from file: 72)
DIALOG(R)File 72:EMBASE

8648850 EMBASE No: 92329379
The potential of cytokines as adjuvants
Heath A.W.; Playfair J.H.L.
DNAX Research Institute, 901 California Avenue, Palo Alto, CA 94304 USA
AIDS RES. HUM. RETROVIRUSES (USA) , 1992, 8/8 (1401-1403)
CODEN: ARHRE ISSN: 0889-2229
LANGUAGES: English

14/3/19 (Item 19 from file: 72)
DIALOG(R)File 72:EMBASE

8483697 EMBASE No: 92159564
Cytokines as immunological adjuvants

Heath A.W.; Playfair J.H.L.
Department of Immunology, DNAX Research Institute, 901 California Ave., Palo Alto, CA 94304 USA
VACCINE (United Kingdom) , 1992, 10/7 (427-434)
CODEN: VACCD ISSN: 0264-410X ADONIS ORDER NUMBER: 0264410X9200237P
LANGUAGES: English SUMMARY LANGUAGES: English

14/3/20 (Item 20 from file: 72)
DIALOG(R)File 72:EMBASE

8154651 EMBASE No: 91184010
Problem-focused supervision: Rationale, exemplification, and limitations
Storm C.L.; **Heath A.W.**
Pacific Lutheran University, Tacoma, WA USA
J. FAMILY PSYCHOTHER. (USA) , 1991, 2/1 (55-70)
CODEN: JFAPE ISSN: 0897-5353
LANGUAGES: English

14/3/21 (Item 21 from file: 72)
DIALOG(R)File 72:EMBASE

8105983 EMBASE No: 91137138
Effects of interferon gamma and saponin on lymphocyte traffic are inversely related to adjuvanticity and enhancement of MHC class II expression
Heath A.W.; Nyan O.; Richards C.E.; Playfair J.H.L.
Department of Immunology, University College, London W1P 9PG United Kingdom
INT. IMMUNOL. (United Kingdom) , 1991, 3/3 (285-292)
CODEN: INIME ISSN: 0953-8178 ADONIS ORDER NUMBER: 095381789100047F
LANGUAGES: English

14/3/22 (Item 22 from file: 72)
DIALOG(R)File 72:EMBASE

8010495 EMBASE No: 91042337
Monoclonal antibodies mediating viable immunofluorescence and protection against Trypanosoma cruzi infection
Heath A.W.; Martins M.S.; Hudson L.
Department of Immunology, St. George's Hospital Medical School, London United Kingdom
TROP. MED. PARASITOL. (Germany, Federal Republic of) , 1990, 41/4 (425-428)
CODEN: TMPAE ISSN: 0177-2392
LANGUAGES: English

14/3/23 (Item 23 from file: 72)
DIALOG(R)File 72:EMBASE

7975844 EMBASE No: 91005822
Conjugation of interferon-gamma to antigen enhances its adjuvanticity
Heath A.W.; Playfair J.H.L.
University College and Middlesex School of Medicine, London United Kingdom
IMMUNOLOGY (United Kingdom) , 1990, 71/3 (454-456)
CODEN: IMMUA ISSN: 0019-2805
LANGUAGES: English

14/3/24 (Item 24 from file: 72)
DIALOG(R)File 72:EMBASE
(c) 1998 Elsevier Science B.V. All rts. reserv.

7755841 EMBASE No: 90185375
Cytokines and infection
Heath A.W.
Department of Immunology, University College and Middlesex School of Medicine, London United Kingdom
CURR. OPIN. IMMUNOL. (United Kingdom) , 1989/90, 2/3 (380-384)
CODEN: COPIE ISSN: 0952-7915
LANGUAGES: English

14/3/25 (Item 25 from file: 72)
DIALOG(R)File 72:EMBASE
(c) 1998 Elsevier Science B.V. All rts. reserv.

7481504 EMBASE No: 89203733
Interferon-gamma as an adjuvant in immunocompromised mice
Heath A.W.; Devey M.E.; Brown I.N.; Richards C.E.; Playfair J.H.L.
Department of Immunology, U.C.S.M., St Mary's Hospital Medical School, London United Kingdom
IMMUNOLOGY (United Kingdom) , 1989, 67/4 (520-524)
CODEN: IMMUA ISSN: 0019-2805
LANGUAGES: English

14/3/26 (Item 26 from file: 72)
DIALOG(R)File 72:EMBASE
(c) 1998 Elsevier Science B.V. All rts. reserv.

7252775 EMBASE No: 88252708
Systemic treatment of substance abuse: A graduate course
Heath A.W.; Atkinson B.J.
Department of Human and Family Resources, Northern Illinois University, DeKalb, IL 60115-2854 USA
J. MARITAL FAM. THER. (USA) , 1988, 14/4 (411-418)
CODEN: JMFTD ISSN: 0194-472X
LANGUAGES: English

14/3/27 (Item 27 from file: 72)
DIALOG(R)File 72:EMBASE
(c) 1998 Elsevier Science B.V. All rts. reserv.

6217765 EMBASE No: 86212828
Cold-adapted reassortants of influenza A virus: Pathogenicity of A/Ann Arbor/6/60 x A/Alaska/6/77 reassortant viruses in vivo and in vitro
Heath A.W.; Maassab H.F.; Odagiri T.; et al.
Department of Virology, University of Sheffield Medical School, Sheffield UNITED KINGDOM
ARCH. VIROL. (AUSTRIA) , 1986, 91/1-2 (53-60)
CODEN: ARVID
LANGUAGES: ENGLISH
? t s15/3/all

15/3/1 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 1998 American Chemical Society. All rts. reserv.

128126847 CA: 128(11)126847m JOURNAL

Enhancement of T cell-independent immune responses in vivo by CD40 antibodies
AUTHOR(S): Dullforce, Per; Sutton, Debbie C.; Heath, Andrew W.
LOCATION: Division of Molecular and Genetic Medicine, Sheffield Institute for Vaccine Studies, University of Sheffield Medical School, Sheffield, UK, S10 2RX
JOURNAL: Nat. Med. (N. Y.) DATE: 1998 VOLUME: 4 NUMBER: 1 PAGES: 88-91 CODEN: NAMEFI ISSN: 1078-8956 LANGUAGE: English PUBLISHER: Nature America

15/3/2 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

127107684 CA: 127(8)107684u JOURNAL
Large scale comparison of adjuvant effects on immunogenicity and protection in a Herpes Simplex virus type 1 vaccination model
AUTHOR(S): Simms, Jack R.; Heath, Andrew W.; Richardson, Vernon J.; Jennings, Roy
LOCATION: Dep. Med. Microbiology, Univ. Sheffield Med. School, Sheffield, UK, S10 2RX
JOURNAL: Biochem. Soc. Trans. DATE: 1997 VOLUME: 25 NUMBER: 2 PAGES: 272S CODEN: BCSTB5 ISSN: 0300-5127 LANGUAGE: English PUBLISHER: Portland Press

15/3/3 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

127093877 CA: 127(7)93877v JOURNAL
Enhancement of immunogenicity of recombinant antigens by production of a cytokine-antigen fusion protein for vaccination
AUTHOR(S): McCormick, Adele L.; Thomas, Mark S.; Heath, Andrew W.
LOCATION: Dep. Medical Microbiology, Univ. Sheffield Med. School, Sheffield, UK, S10 2RX
JOURNAL: Biochem. Soc. Trans. DATE: 1997 VOLUME: 25 NUMBER: 2 PAGES: 297S CODEN: BCSTB5 ISSN: 0300-5127 LANGUAGE: English PUBLISHER: Portland Press

15/3/4 (Item 4 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

126156211 CA: 126(12)156211a JOURNAL
CD40 signaling induces interleukin-4-independent IgE switching in vivo
AUTHOR(S): Ferlin, Walter G.; Severinson, Eva; Stroem, Lena; Heath, Andrew W.; Coffman, Robert L.; Ferrick, David A.; Howard, Maureen C.
LOCATION: DNAX Research Inst., Palo Alto, CA, 94304, USA
JOURNAL: Eur. J. Immunol. DATE: 1996 VOLUME: 26 NUMBER: 12 PAGES: 2911-2915 CODEN: EJIMAF ISSN: 0014-2980 LANGUAGE: English PUBLISHER: VCH

15/3/5 (Item 5 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

125325452 CA: 125(25)325452s JOURNAL
Interleukin 13 and related cytokines
AUTHOR(S): McKenzie, Andrew N. J.; Heath, Andrew W.
LOCATION: MRC Laboratory Molecular Biology, Cambridge, UK, CB2 2QH
JOURNAL: Blood Cell Biochem. DATE: 1996 VOLUME: 7 NUMBER:

Hematopoietic Cell Growth Factors and Their Receptors PAGES: 41-50
CODEN: BCEBEK ISSN: 1078-0491 LANGUAGE: English

15/3/6 (Item 6 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

125299333 CA: 125(23)299333g JOURNAL
Differential activation of the ERK, JNK, and p38 mitogen-activated protein kinases by CD40 and the B cell antigen receptor
AUTHOR(S): Sutherland, Claire L.; Heath, Andrew W.; Pelech, Steven L.; Young, Peter R.; Gold, Michael R.
LOCATION: Dep. Microbiol. Immunol., Univ. British Columbia, Vancouver, BC , Can., V6T 1Z3
JOURNAL: J. Immunol. DATE: 1996 VOLUME: 157 NUMBER: 8 PAGES: 3381-3390 CODEN: JOIMA3 ISSN: 0022-1767 LANGUAGE: English

15/3/7 (Item 7 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

124052966 CA: 124(5)52966t JOURNAL
Cytokines as immunological adjuvants
AUTHOR(S): Heath, Andrew W.
LOCATION: Medical School, University Sheffield, Sheffield, UK, S10 2RX
JOURNAL: Pharm. Biotechnol. DATE: 1995 VOLUME: 6 NUMBER: Vaccine Design PAGES: 645-58 CODEN: PHBIEB ISSN: 1078-0467 LANGUAGE: English

15/3/8 (Item 8 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

123283144 CA: 123(21)283144u JOURNAL
The effect of antigen dose on CD4+ T helper cell phenotype development in a T cell receptor-.alpha..beta.-transgenic model
AUTHOR(S): Hosken, Nancy A.; Shibuya, Kazuko; Heath, Andrew W.; Murphy, Kenneth M.; O'Garra, Anne
LOCATION: Department of Immunology, DNAX Research Institute, Palo Alto, CA, 94304, USA
JOURNAL: J. Exp. Med. DATE: 1995 VOLUME: 182 NUMBER: 5 PAGES: 1579-84
CODEN: JEMEAV ISSN: 0022-1007 LANGUAGE: English

15/3/9 (Item 9 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

123030894 CA: 123(3)30894v JOURNAL
Signaling through murine CD38 is impaired in antigen receptor-unresponsive B cells
AUTHOR(S): Lund, Frances E.; Solvason, Nanette W.; Cooke, Michael P.; Heath, Andrew W.; Grimaldi, J. Christopher; Parkhouse, R. M. E.; Goodnow, Christopher C.; Howard, Maureen C.
LOCATION: DNAX Research Institute, Palo Alto, CA, 94304, USA
JOURNAL: Eur. J. Immunol. DATE: 1995 VOLUME: 25 NUMBER: 5 PAGES: 1338-45 CODEN: EJIMAF ISSN: 0014-2980 LANGUAGE: English

15/3/10 (Item 10 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

122237209 CA: 122(19)237209a JOURNAL
CD38 unresponsiveness of xid B cells implicates Bruton's tyrosine kinase (btk) as a regulator of CD38 induced signal transduction
AUTHOR(S): Santos-Argumedo, Leopoldo; Lund, Frances E.; Heath, Andrew W.; Solvason, Nanette; Wu, Wei Wei; Grimaldi, Christopher; Parkhouse, R. M. E.; Howard, Maureen
LOCATION: DNAX Research Institute, Palo Alto, CA, 94304, USA
JOURNAL: Int. Immunol. DATE: 1995 VOLUME: 7 NUMBER: 2 PAGES: 163-70
CODEN: INIMEN ISSN: 0953-8178 LANGUAGE: English

15/3/11 (Item 11 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

121155623 CA: 121(13)155623w JOURNAL
Antibodies to murine CD40 protect normal and malignant B cells from induced growth arrest
AUTHOR(S): Santos-Argumedo, Leopoldo; Gordon, John; Heath, Andrew W.; Howard, Maureen
LOCATION: DNAX Res. Inst., Palo Alto, CA, 94304, USA
JOURNAL: Cell. Immunol. DATE: 1994 VOLUME: 156 NUMBER: 2 PAGES: 272-85 CODEN: CLIMB8 ISSN: 0008-8749 LANGUAGE: English

15/3/12 (Item 12 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

121155203 CA: 121(13)155203j JOURNAL
Monoclonal antibodies to murine CD40 define two distinct functional epitopes
AUTHOR(S): Heath, Andrew W.; Wu, Wei Wei; Howard, Maureen C.
LOCATION: DNAX Research Institute, Palo Alto, CA, USA
JOURNAL: Eur. J. Immunol. DATE: 1994 VOLUME: 24 NUMBER: 8 PAGES: 1828-34 CODEN: EJIMAF ISSN: 0014-2980 LANGUAGE: English

15/3/13 (Item 13 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

121006642 CA: 121(1)6642z JOURNAL
Cytokines and the rational choice of immunological adjuvants
AUTHOR(S): Heath, Andrew W.
LOCATION: DNAX Res. Inst., Palo Alto, CA, 94025, USA
JOURNAL: Cancer Biother. DATE: 1994 VOLUME: 9 NUMBER: 1 PAGES: 1-6
CODEN: CNBTEB ISSN: 1062-8401 LANGUAGE: English

15/3/14 (Item 14 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

120268202 CA: 120(21)268202f PATENT
CD40 ligand, anti CD40 antibodies, and soluble CD40 and their use in the inhibition of proliferation of lymphoma cells
INVENTOR(AUTHOR): Heath, Andrew W.; Howard, Maureen; Lanier, Lewis L.
LOCATION: USA
ASSIGNEE: Schering Corp.
PATENT: PCT International ; WO 9404570 A1 DATE: 940303
APPLICATION: WO 93US7673 (930819) *US 934371 (920821)
PAGES: 46 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07K-015/06A; C07K-015/28B; A61K-037/02B DESIGNATED COUNTRIES: AU; BB; BG; BR; BY; CA; CZ; FI; HU; JP; KR; KZ; LK; MG; MN; MW; NO; NZ; PL; RO; RU; SD; SK; UA; US;

VN DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC ; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE; SN; TD; TG

15/3/15 (Item 15 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

120104514 CA: 120(9)104514h JOURNAL
Immunoglobulin signal transduction guides the specificity of B cell-T cell interactions and is blocked in tolerant self-reactive B cells
AUTHOR(S): Cooke, Michael P.; Heath, Andrew W.; Shokat, Kevan M.; Zeng, Yongjun; Finkelman, Fred D.; Linsley, Peter S.; Howard, Maureen; Goodnow, Christopher C.
LOCATION: Howard Hughes Med. Inst., Stanford Univ., Stanford, CA, 94305, USA
JOURNAL: J. Exp. Med. DATE: 1994 VOLUME: 179 NUMBER: 2 PAGES: 425-38
CODEN: JEMEAV ISSN: 0022-1007 LANGUAGE: English

15/3/16 (Item 16 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

120028934 CA: 120(3)28934c JOURNAL
Antibodies to murine CD40 stimulate normal B lymphocytes but inhibit proliferation of B lymphoma cells
AUTHOR(S): Heath, Andrew W.; Chang, Ray; Harada, Nobuyuki; Santos-Argumedo, Leopoldo; Gordon, John; Hannum, Charles; Campbell, David; Shanafelt, Armen B.; Clark, Edward A.; et al.
LOCATION: Res. Inst., DNAX, Palo Alto, CA, 94304, USA
JOURNAL: Cell. Immunol. DATE: 1993 VOLUME: 152 NUMBER: 2 PAGES: 468-80 CODEN: CLIMB8 ISSN: 0008-8749 LANGUAGE: English

15/3/17 (Item 17 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

120028852 CA: 120(3)28852z JOURNAL
Expression cloning of a cDNA encoding a novel murine B cell activation marker. Homology to human CD38
AUTHOR(S): Harada, Nobuyuki; Santos-Argumedo, Leopoldo; Chang, Ray; Grimaldi, J. Christopher; Lund, Frances E.; Brannan, Camilynn I.; Copeland, Neal G.; Jenkins, Nancy A.; Heath, Andrew W.; et al.
LOCATION: Res. Inst., DNAX, Palo Alto, CA, 94304, USA
JOURNAL: J. Immunol. DATE: 1993 VOLUME: 151 NUMBER: 6 PAGES: 3111-18
CODEN: JOIMA3 ISSN: 0022-1767 LANGUAGE: English

15/3/18 (Item 18 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

120006547 CA: 120(1)6547b JOURNAL
Expression of the murine interleukin-4 gene in an attenuated aroA strain of Salmonella typhimurium: Persistence and immune response in BALB/c mice and susceptibility to macrophage killing
AUTHOR(S): Denich, Kenneth; Borlin, Patrick; O'Hanley, Peter; Howard, Maureen; Heath, Andrew W.
LOCATION: Stanford Univ., Stanford, CA, 94305-5402, USA
JOURNAL: Infect. Immun. DATE: 1993 VOLUME: 61 NUMBER: 11 PAGES: 4818-27 CODEN: INFIBR ISSN: 0019-9567 LANGUAGE: English

15/3/19 (Item 19 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
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118057539 CA: 118(7)57539s JOURNAL
The potential of cytokines as adjuvants
AUTHOR(S): Heath, Andrew W.; Playfair, John H. L.
LOCATION: DNAX Res. Inst., Palo Alto, CA, 94304, USA
JOURNAL: AIDS Res. Hum. Retroviruses DATE: 1992 VOLUME: 8 NUMBER: 8
PAGES: 1401-3 CODEN: ARHRE7 ISSN: 0889-2229 LANGUAGE: English

15/3/20 (Item 20 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 1998 American Chemical Society. All rts. reserv.

115277605 CA: 115(25)277605p CONFERENCE PROCEEDING
Early administration of interferon-.gamma. as an adjuvant: an effect on a T-helper subpopulation?
AUTHOR(S): Heath, Andrew W.; Playfair, John H. L.
LOCATION: Dep. Immunol., Univ. Coll., London, UK, W1P 9PG
JOURNAL: Vaccines 91: Mod. Approaches New Vaccines Incl. Prev. AIDS, (Annu. Meet. Mod. Approaches New Vaccines), 8th EDITOR: Chanock, Robert M (Ed), DATE: 1991 PAGES: 351-4 CODEN: 57HGAV LANGUAGE: English
MEETING DATE: 900000 PUBLISHER: Cold Spring Harbor Lab.,Plainview, N. Y
? s (s13 or s14 or s15) and (cd40L or cd40(W)ligand or gp39)

```
            46  S13
            27  S14
            20  S15
          1515  CD40L
          5612  CD40
        192014  LIGAND
          2178  CD40(W)LIGAND
           392  GP39
    S17     3  (S13 OR S14 OR S15) AND (CD40L OR CD40(W)LIGAND OR GP39)
```

? rd s17

>>>Duplicate detection is not supported for File 351.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records

```
    S18     3  RD S17 (unique items)
```

? t s18/7/all

18/7/1 (Item 1 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
(c) 1998 BIOSIS. All rts. reserv.

14107118 BIOSIS Number: 01107118
Suppression of alloantibody responses by **CD40 ligand** expression
McCormick A L; Thomas M S; **Heath A W**
Dep. Medical Microbiol., Univ. Sheffield Medical Sch., Beech Hill Rd., Sheffield S10 2RX, UK
Immunology 92 (SUPPL. 1). 1997. 45.
Full Journal Title: 5th Annual Congress of the British Society for Immunology, Brighton, England, UK, December 2-5, 1997. Immunology
ISSN: 0019-2805
Language: ENGLISH
Print Number: Biological Abstracts/RRM Vol. 050 Iss. 003 Ref. 041030

18/7/2 (Item 1 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)
(c) 1998 American Chemical Society. All rts. reserv.

120268202 CA: 120(21)268202f PATENT
CD40 ligand, anti CD40 antibodies, and soluble CD40 and their use in the inhibition of proliferation of lymphoma cells
INVENTOR(AUTHOR): Heath, Andrew W.; Howard, Maureen; Lanier, Lewis L.
LOCATION: USA
ASSIGNEE: Schering Corp.
PATENT: PCT International ; WO 9404570 A1 DATE: 940303
APPLICATION: WO 93US7673 (930819) *US 934371 (920821)
PAGES: 46 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07K-015/06A; C07K-015/28B; A61K-037/02B DESIGNATED COUNTRIES: AU; BB; BG; BR; BY; CA; CZ; FI; HU; JP; KR; KZ; LK; MG; MN; MW; NO; NZ; PL; RO; RU; SD; SK; UA; US; VN DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC ; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE; SN; TD; TG
SECTION:
CA215002 Immunochemistry
CA201XXX Pharmacology
IDENTIFIERS: CD40 antigen antibody lymphoma proliferation inhibitor
DESCRIPTORS:
Gene,animal...
cDNA, for sol. CD40 analogs, expression in L and COS7 and Sf9 cells of
Lymphocyte,B-cell...
CD40 ligand for, purifn. of and cloning of gene for
Lymphoma...
CD40+, sol. CD40 analogs and ligands and antibodies to, for inhibition of proliferation of
Gene,animal...
for CD40 ligand of B-cells
Plasmid and Episome...
pMe18S-FLCD40, cDNA for sol. CD40 analog on, expression in L cells of
Antigens,CD40...
sol. analogs and ligands and antibodies to, in inhibition of proliferation of lymphoma cells
Neoplasm inhibitors,lymphoma...
sol. CD40 analogs and ligands and antibodies as
Lymphoma,B-cell...
sol. CD40 analogs and ligands and antibodies to, for inhibition of proliferation of
Antibodies... Antibodies,monoclonal...
to sol. CD40, inhibition of B-lymphoma proliferation by

18/7/3 (Item 1 from file: 351)
DIALOG(R)File 351:DERWENT WPI
(c)1998 Derwent Info Ltd. All rts. reserv.

009803260
WPI Acc No: 94-083114/199410
New soluble form of CD40 and B cell **CD40 ligand** - for inhibiting growth of CD40 positive malignant, esp B lymphoma, cells or reducing T cell activity against CD40 positive cells
Patent Assignee: SCHERING CORP (SCHE)
Inventor: **HEATH A W**; HOWARD M; LANIER L L
Number of Countries: 043 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
WO 9404570	A1	19940303	WO 93US7673	A	19930819	C07K-015/06	199410 B
AU 9350984	A	19940315	AU 9350984	A	19930819	C07K-015/06	199428

Priority Applications (No Type Date): US 92934371 A 19920821
Cited Patents: 3.Jnl.Ref
Patent Details:

Patent	Kind	Lan	Pg	Filing Notes	Application	Patent

WO 9404570 A1 E 46
Designated States (National): AU BB BG BR BY CA CZ FI HU JP KR KZ LK MG MN MW NO NZ PL RO RU SD SK UA US VN
Designated States (Regional): AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
AU 9350984 A Based on WO 9404570

Abstract (Basic): WO 9404570 A

A soluble form (I) of CD40 which lacks (most of) the cytoplasmic and/or transmembrane domains of wild type CD40 is new. Also new are (1) purified B-cell **CD40 ligand**(L) and (2) DNA encoding (L).

USE - (I), and ligands that bind CD40, are useful (a) for inhibiting proliferation of CD40 positive malignant cells (esp. B lymphoma cells, but also leukaemia and carcinoma) and (b) reducing activity of T cells against CD40 positive cells (e.g. in cases of autoimmune diseases, delayed hypersensitivity reactions or transplant rejection). Also CD40-negative malignant cells can be made more immunogenic to T cells by transforming them with DNA encoding human CD40, which is then expressed on the surface. (I) and CD40 ligands do not inhibit proliferation of normal B cells.

Dwg.0/0

Derwent Class: B04; D16
International Patent Class (Main): C07K-015/06
International Patent Class (Additional): A61K-037/02; C07K-015/28

```
  *  thereof, nor any of their contractors, subcontractors or   *
  *  employees make any warranty, expressed or implied,         *
  *  including any warranty of marketability of fitness for a   *
  *  particular purpose; nor assumes any legal liability or     *
  *  responsibility for any party's use, or the results of      *
  *  such, of the data.                                         *
  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
  *                Help Desk --> 703-305-9000                   *
  *                                                             *
  *    The Help Desk is staffed for APS support 7 days/week.    *
  *      Monday through Friday:      6:30am - 9:00pm            *
  *      Saturday, Sunday, Holidays: 8:30am - 5:00 pm           *
  *                                                             *
  *    The Help Desk staff at this number will handle all APS   *
  *    related questions.                                       *
  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
  *    >>>>>>>>>>>>> NEW SUNDAY HOURS !!! <<<<<<<<<<<<<         *
  *                                                             *
  *    The APS is available:                                    *
  *            6:30am - 9:00pm Monday through Friday            *
  *            7:30am - 5:00pm Saturday, Sunday, Holidays       *
  *                                                             *
  *      APS is unavailable Thanksgiving Day, Christmas Day,    *
  *      and New Year's Day.                                    *
  *                                                             *
  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
FILE 'USPAT' ENTERED AT 07:58:34 ON 26 MAY 1998

  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
  *              W E L C O M E   T O   T H E                  *
  *         U. S.   P A T E N T   T E X T   F I L E           *
  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *

=> (antibod?)(P)(cd40 or bp50)(P)(adjuvant? or vaccin?)

'(ANTIBOD?)(P)(CD40' IS NOT A RECOGNIZED COMMAND

=> s (antibod?)(P)(cd40 or bp50)(P)(adjuvant? or vaccin?)

         28261 ANTIBOD?
            91 CD40
             7 BP50
         32634 ADJUVANT?
          8061 VACCIN?
L1           4 (ANTIBOD?)(P)(CD40 OR BP50)(P)(ADJUVANT? OR VACCIN?)

=> d l1 1-4


1.  5,756,096, May 26, 1998, Recombinant antibodies for human therapy;
Roland A. Newman, et al., 424/154.1, 133.1, 141.1; 530/387.1 [IMAGE
AVAILABLE]

2.  5,677,165, Oct. 14, 1997, Anti-CD40 monoclonal antibodies capable of
blocking B-cell activation; Mark de Boer, et al., 435/343.1, 70.21,
172.2; 530/388.22, 388.73 [IMAGE AVAILABLE]

3.  5,596,072, Jan. 21, 1997, Method of refolding human IL-13; Janice
```

Culpepper, et al., 530/351; 424/85.2; 435/69.1; 530/402, 412; 930/141 [IMAGE AVAILABLE]

4. 5,565,321, Oct. 15, 1996, Detection of mutations in a CD40 ligand gene; Melanie K. Spriggs, et al., 435/6, 7.1, 91.1; 536/23.1, 23.5, 24.3, 24.31; 935/77 [IMAGE AVAILABLE]

=> d l1 1-4 date

L1: 1 of 4

TITLE: Recombinant antibodies for human therapy
US PAT NO: 5,756,096 [IMAGE AVAILABLE] DATE ISSUED: May 26, 1998
APPL-NO: 08/476,237 DATE FILED: Jun. 7, 1995
REL-US-DATA: Continuation-in-part of Ser. No. 379,072, Jan. 25, 1995, Pat. No. 5,658,570, which is a continuation of Ser. No. 912,292, Jul. 10, 1992, abandoned, which is a continuation-in-part of Ser. No. 856,281, Mar. 23, 1992, abandoned, which is a continuation-in-part of Ser. No. 735,064, Jul. 25, 1991, abandoned.

L1: 2 of 4

TITLE: Anti-CD40 monoclonal antibodies capable of blocking B-cell activation
US PAT NO: 5,677,165 [IMAGE AVAILABLE] DATE ISSUED: Oct. 14, 1997
APPL-NO: 08/070,158 DATE FILED: May 28, 1993
REL-US-DATA: Continuation-in-part of Ser. No. 910,222, Jul. 9, 1992, abandoned.

L1: 3 of 4

TITLE: Method of refolding human IL-13
US PAT NO: 5,596,072 [IMAGE AVAILABLE] DATE ISSUED: Jan. 21, 1997
APPL-NO: 08/012,543 DATE FILED: Feb. 1, 1993
REL-US-DATA: Continuation-in-part of Ser. No. 933,416, Aug. 21, 1992, abandoned.

L1: 4 of 4

TITLE: Detection of mutations in a CD40 ligand gene
US PAT NO: 5,565,321 [IMAGE AVAILABLE] DATE ISSUED: Oct. 15, 1996
APPL-NO: 08/184,422 DATE FILED: Jan. 21, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 9,258, Jan. 22, 1993, abandoned.

=> d l1 1-4 kwic

US PAT NO: 5,756,096 [IMAGE AVAILABLE] L1: 1 of 4

DETDESC:

DETD(26)

In using the subject CE9.1 monoclonal **antibody** for the treatment of autoimmune disorders, including for example rheumatoid arthritis, this **antibody** may be administered by itself or in combination with other compounds suitable for treatment of the particular disease condition. For example, the subject **antibody** may be administered in combination with other proteins, for example monoclonal **antibody** soluble receptor proteins to TNF-alpha, monoclonal **antibodies** to IL2 receptor, monoclonal **antibodies** and receptor fusion proteins which antagonize the **CD40**/gp39 interaction and CTLA 4-Ig in monoclonal **antibodies**

which antagonize the B7/CD28 interaction. Also, in the case of treatment of rheumatoid arthritis, the subject **antibody** may be administered in combination with other therapeutics, for example Rapamycin, Leflunomide, Tenidap, RS-61443 (Mycophenolate Mofetil), Surenyl (sodium Hyaluronate), anti-TCR (V.beta.17) peptide **vaccine**, Anerva X (anti-MHC **vaccine**), and extracorporeal protein A immunoabsorbants or combinations thereof. Additionally, the subject **antibody** may be administered in combination with other **antibodies** produced according to the invention or known in the art which are specific to human CD4. This may result in synergistic effects, for example, if these **antibodies** bind to different epitopes of the CD4 protein.

US PAT NO: 5,677,165 [IMAGE AVAILABLE] L1: 2 of 4

DETDESC:

DETD(14)

Polyclonal sera may be prepared by conventional methods. In general, a solution containing the **CD40** antigen is first used to immunize a suitable animal, preferably a mouse, rat, rabbit or goat. Rabbits and goats are. . . the preparation of polyclonal sera due to the volume of serum obtainable, and the availability of labeled anti-rabbit and anti-goat **antibodies**. Immunization is generally performed by mixing or emulsifying the antigen-containing solution in saline, preferably in an **adjuvant** such as Freund's complete **adjuvant**, and injecting the mixture or emulsion parenterally (generally subcutaneously or intramuscularly). A dose of 50-200 .mu.g/injection is typically sufficient. Immunization. . . is generally boosted 2-6 weeks later with one or more injections of the protein in saline, preferably using Freund's incomplete **adjuvant**. One may alternatively generate **antibodies** by in vitro immunization using methods known in the art, which for the purposes of this invention is considered equivalent. . .

US PAT NO: 5,596,072 [IMAGE AVAILABLE] L1: 3 of 4

DETDESC:

DETD(231)

Eight . . . female Lewis rats were obtained from Harlan Sprague-Dawley (Indianapolis, Ind.). These rats were immunized intaperitoneally with 10 .mu.g of soluble **CD40** in complete Freund's **adjuvant** followed by boosts of 10, 10, 10, and 50 .mu.g of soluble **CD40** in incomplete Freund's **adjuvant** at 3, 4.5, 6, and 8.5 weeks, respectively. A final boost in saline was injected at 12 weeks. Test bleeds were evaluated for anti-**CD40 antibody** content by ELISA.

US PAT NO: 5,565,321 [IMAGE AVAILABLE] L1: 4 of 4

DETDESC:

DETD(24)

CD40-L KO mice are likely to be of great interest to scientists investigating the cognate interactions between T and B cells in thymus-dependent **antibody** responses, as well as various aspects of immunoglobulin isotype switching. The role of **CD40**-L in human X-linked hyper-IgM syndrome indicates that **CD40**-L KO mice would be a valuable asset for testing possible treatments (i.e. administration of soluble, recombinant ligand) for hyper IgM. Additionally, **CD40**-L knockout mice are of interest for many different types of investigation, in that these animals have an exquisitely defined genetic defect that is expected to disable one specific cellular interaction necessary for an immune response. Thus, **CD40**-L KO mice are expected to be useful as

models for testing **vaccine** preparations or immune response modifiers, in defining the role of T cells and B cells in various diseases and syndromes. . .

=> e ledbetter/in

E#	FILE	FREQUENCY	TERM
E1	USPAT	1	LEDANY, ORI/IN
E2	USPAT	1	LEDARD, CLAUDE/IN
E3	USPAT	0 -->	LEDBETTER/IN
E4	USPAT	1	LEDBETTER, BUFORD B/IN
E5	USPAT	7	LEDBETTER, CARL J/IN
E6	USPAT	1	LEDBETTER, CARL S JR/IN
E7	USPAT	1	LEDBETTER, CARL W/IN
E8	USPAT	1	LEDBETTER, CLYDE S/IN
E9	USPAT	1	LEDBETTER, CRAIG A/IN
E10	USPAT	2	LEDBETTER, DANIEL R/IN
E11	USPAT	1	LEDBETTER, ELMER W/IN
E12	USPAT	1	LEDBETTER, FERMAN/IN

=> e

E13	USPAT	3	LEDBETTER, FRANK E III/IN
E14	USPAT	1	LEDBETTER, GARY A/IN
E15	USPAT	1	LEDBETTER, HAROLD J/IN
E16	USPAT	6	LEDBETTER, HARVEY D/IN
E17	USPAT	2	LEDBETTER, JAMES A/IN
E18	USPAT	1	LEDBETTER, JAMES W/IN
E19	USPAT	13	LEDBETTER, JEFFREY A/IN
E20	USPAT	1	LEDBETTER, JENNINGS M/IN
E21	USPAT	2	LEDBETTER, JERRY T/IN
E22	USPAT	1	LEDBETTER, JOHN JR/IN
E23	USPAT	1	LEDBETTER, MARGARET S/IN
E24	USPAT	1	LEDBETTER, MARSHALL D/IN

=> s e19

L2 13 "LEDBETTER, JEFFREY A"/IN

=> d l2 1-13

1. 5,747,037, May 5, 1998, Anti-GP39 antibodies; Randolph J. Noelle, et al., 424/154.1, 130.1, 141.1, 143.1, 144.1, 153.1, 173.1; 435/70.21, 172.2, 326, 332, 334, 343, 343.1, 343.2, 346; 530/387.1, 388.1, 388.2, 388.22, 388.7, 388.73, 388.75 [IMAGE AVAILABLE]

2. 5,721,108, Feb. 24, 1998, Chimeric antibody with specificity to human B cell surface antigen; Randy R. Robinson, et al., 435/7.23; 424/1.49, 9.34, 133.1; 435/7.24; 436/518; 530/387.3, 388.73, 391.1, 391.3 [IMAGE AVAILABLE]

3. 5,709,859, Jan. 20, 1998, Mixed specificity fusion proteins; Alejandro A. Aruffo, et al., 424/134.1, 136.1, 178.1; 435/69.7; 530/387.3, 388.22, 808, 866 [IMAGE AVAILABLE]

4. 5,677,180, Oct. 14, 1997, Chimeric antibody with specificity to human B cell surface antigen; Randy R. Robinson, et al., 435/328, 69.6, 70.21, 172.3, 254.2, 343.1 [IMAGE AVAILABLE]

5. 5,637,481, Jun. 10, 1997, Expression vectors encoding bispecific fusion proteins and methods of producing biologically active bispecific fusion proteins in a mammalian cell; **Jeffrey A. Ledbetter**, et al., 435/69.6, 69.1, 69.7, 172.1, 320.1, 326, 328, 332 [IMAGE AVAILABLE]

6. 5,580,756, Dec. 3, 1996, B7IG fusion protein; Peter S. Linsley, et al., 435/69.7, 91.1; 530/350, 387.1, 387.3, 395; 536/23.4 [IMAGE AVAILABLE]

7. 5,540,926, Jul. 30, 1996, Soluble and its use in B cell stimulation; Alejandro Aruffo, et al., 424/153.1, 173.1, 192.1; 435/69.1, 69.3, 69.7, 252.3, 320.1; 514/12; 530/350, 387.1 [IMAGE AVAILABLE]

8. 5,521,288, May 28, 1996, CD28IG fusion protein; Peter S. Linsley, et al., 530/387.3; 435/7.2, 7.92, 69.1, 69.7, 91.1, 252.3, 252.33, 320.1; 530/300, 350, 387.1, 395, 409, 866, 867, 868; 536/23.1, 23.4, 23.53 [IMAGE AVAILABLE]

9. 5,500,362, Mar. 19, 1996, Chimeric antibody with specificity to human B cell surface antigen; Randy R. Robinson, et al., 435/7.23; 424/133.1, 153.1, 155.1; 435/7.24, 70.21, 172.2; 530/387.3, 388.73 [IMAGE AVAILABLE]

10. 5,434,131, Jul. 18, 1995, Chimeric CTLA4 receptor and methods for its use; Peter S. Linsley, et al., 514/2; 424/133.1; 514/12; 530/350, 866, 868; 935/10 [IMAGE AVAILABLE]

11. 5,247,069, Sep. 21, 1993, Ligands and methods for augmenting B-cell proliferation; **Jeffrey A. Ledbetter**, et al., 530/350, 380, 395, 829 [IMAGE AVAILABLE]

12. 5,182,368, Jan. 26, 1993, Ligands and methods for augmenting B-cell proliferation; **Jeffrey A. Ledbetter**, et al., 530/388.73; 435/188; 530/350, 351, 391.3, 391.7, 866 [IMAGE AVAILABLE]

13. 4,677,061, Jun. 30, 1987, T-cell lymphocyte subset monitoring of immunologic disease; Lynn M. Rose, et al., 435/7.24, 7.5, 29, 34, 39, 968; 436/501, 543, 546 [IMAGE AVAILABLE]

=> s l2 and (cd40 or bp50)

```
            91 CD40
             7 BP50
L3           7 L2 AND (CD40 OR BP50)
```

=> d l3 1-7

1. 5,747,037, May 5, 1998, Anti-GP39 antibodies; Randolph J. Noelle, et al., 424/154.1, 130.1, 141.1, 143.1, 144.1, 153.1, 173.1; 435/70.21, 172.2, 326, 332, 334, 343, 343.1, 343.2, 346; 530/387.1, 388.1, 388.2, 388.22, 388.7, 388.73, 388.75 [IMAGE AVAILABLE]

2. 5,637,481, Jun. 10, 1997, Expression vectors encoding bispecific fusion proteins and methods of producing biologically active bispecific fusion proteins in a mammalian cell; **Jeffrey A. Ledbetter**, et al., 435/69.6, 69.1, 69.7, 172.1, 320.1, 326, 328, 332 [IMAGE AVAILABLE]

3. 5,580,756, Dec. 3, 1996, B7IG fusion protein; Peter S. Linsley, et al., 435/69.7, 91.1; 530/350, 387.1, 387.3, 395; 536/23.4 [IMAGE AVAILABLE]

4. 5,540,926, Jul. 30, 1996, Soluble and its use in B cell stimulation; Alejandro Aruffo, et al., 424/153.1, 173.1, 192.1; 435/69.1, 69.3, 69.7, 252.3, 320.1; 514/12; 530/350, 387.1 [IMAGE AVAILABLE]

5. 5,521,288, May 28, 1996, CD28IG fusion protein; Peter S. Linsley, et al., 530/387.3; 435/7.2, 7.92, 69.1, 69.7, 91.1, 252.3, 252.33, 320.1; 530/300, 350, 387.1, 395, 409, 866, 867, 868; 536/23.1, 23.4, 23.53 [IMAGE AVAILABLE]

6. 5,247,069, Sep. 21, 1993, Ligands and methods for augmenting B-cell proliferation; **Jeffrey A. Ledbetter**, et al., 530/350, 380, 395, 829 [IMAGE AVAILABLE]

7. 5,182,368, Jan. 26, 1993, Ligands and methods for augmenting B-cell proliferation; **Jeffrey A. Ledbetter**, et al., 530/388.73; 435/188; 530/350, 351, 391.3, 391.7, 866 [IMAGE AVAILABLE]

```
=> s l2 and (anti(w)cd40 or anti(w)bp50)

        152588 ANTI
            91 CD40
            15 ANTI(W)CD40
        152588 ANTI
             7 BP50
             2 ANTI(W)BP50
L4           3 L2 AND (ANTI(W)CD40 OR ANTI(W)BP50)

=> d l4 1-3
```

1. 5,540,926, Jul. 30, 1996, Soluble and its use in B cell stimulation; Alejandro Aruffo, et al., 424/153.1, 173.1, 192.1; 435/69.1, 69.3, 69.7, 252.3, 320.1; 514/12; 530/350, 387.1 [IMAGE AVAILABLE]

2. 5,247,069, Sep. 21, 1993, Ligands and methods for augmenting B-cell proliferation; **Jeffrey A. Ledbetter**, et al., 530/350, 380, 395, 829 [IMAGE AVAILABLE]

3. 5,182,368, Jan. 26, 1993, Ligands and methods for augmenting B-cell proliferation; **Jeffrey A. Ledbetter**, et al., 530/388.73; 435/188; 530/350, 351, 391.3, 391.7, 866 [IMAGE AVAILABLE]

```
=> s l4(P)(adjuvant? or vaccin?)

*WARNING* - PROXIMITY OPERATOR PRECEDENCE LEVEL CONFLICTS OR IS NOT CONSIS
TENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L4(P)(ADJUVANT?'
         32634 ADJUVANT?
          8061 VACCIN?
L5           3 L4(P)(ADJUVANT? OR VACCIN?)

=> s l2 and (anti(w)cd40 or anti(w)bp50)(P)(adjuvant? or vaccin?)

        152588 ANTI
            91 CD40
        152588 ANTI
             7 BP50
         32634 ADJUVANT?
          8061 VACCIN?
             1 (ANTI(W)CD40 OR ANTI(W)BP50)(P)(ADJUVANT? OR VACCIN?)
L6           0 L2 AND (ANTI(W)CD40 OR ANTI(W)BP50)(P)(ADJUVANT? OR VACCIN?
)

=> d l5 1-3
```

1. 5,540,926, Jul. 30, 1996, Soluble and its use in B cell stimulation; Alejandro Aruffo, et al., 424/153.1, 173.1, 192.1; 435/69.1, 69.3, 69.7, 252.3, 320.1; 514/12; 530/350, 387.1 [IMAGE AVAILABLE]

2. 5,247,069, Sep. 21, 1993, Ligands and methods for augmenting B-cell proliferation; **Jeffrey A. Ledbetter**, et al., 530/350, 380, 395, 829 [IMAGE AVAILABLE]

3. 5,182,368, Jan. 26, 1993, Ligands and methods for augmenting B-cell proliferation; **Jeffrey A. Ledbetter**, et al., 530/388.73; 435/188; 530/350, 351, 391.3, 391.7, 866 [IMAGE AVAILABLE]

=> d l5 1-3 kwic

US PAT NO: 5,540,926 [IMAGE AVAILABLE] L5: 1 of 3
INVENTOR: Alejandro Aruffo, Edmonds, WA
Diane Hollenbaugh, Seattle, WA
Jeffrey A. Ledbetter, Seattle, WA

SUMMARY:

BSUM(31)

The role of CD40 in B cell activation is well established. Crosslinking CD40 with **anti-CD40** monoclonal antibodies (mAb) induces B cell aggregation via LFA-I (Gordon et al., 1988, J. Immunol. 140:1425-1430; Barrett et al., 1991,. . . signal which allows B cells to proliferate and undergo class switching when stimulated with the appropriate second signal. For example, **anti-CD40** mAb can synergize with phorbol myristyl acetate (PMA; Gordon et al., 1987, Eur. J. Immunol. 17:1535-1538) or anti-CD20 Mab (Clark. . .

SUMMARY:

BSUM(32)

Crosslinking of **anti-CD40** mAb alone is not sufficient to induce B cell proliferation as demonstrated by the observation that **anti-CD40** mAb immobilized on plastic in conjunction with IL-4 is unable to induce vigorous B cell proliferation (Banchereau et al., 1991, Science 251:70-72). However, **anti-CD40** mAb immobilized on murine L cells transfected with an Fc receptor, CDw32, are able to induce B cell proliferation in. . .

DRAWING DESC:

DRWD(4)

FIGS. . . . to bind either soluble recombinant CD40 (FIGS. 3A and 3B), or soluble recombinant gp39 (FIGS. 3C and 3D), or the **anti-CD40** mAb G28-5 (FIGS. 3E and 3F) as described in the text. Phase (FIGS. 3A, 3C and 3E) and fluorescent (FIGS.. . .

DETDESC:

DETD(15)

In . . . utilized to express the protein-coding sequence. These include, but are not limited to, mammalian cell systems infected with virus (e.g. **vaccinia** virus, adenovirus, etc.) or transfected with plasmid expression vector; insect cell systems infected with virus (e.g. baculovirus); microorganisms such as. . .

DETDESC:

DETD(41)

In . . . embodiments, soluble gp39 may be used to increase an immune response, for example, by acting, effectively, as a type of "**adjuvant**" to increase an immune response to a **vaccine**. Alternatively, soluble gp39 may be used to increase the immune response

of an immunosuppressed individual, such as a person suffering. . .

DETDESC:

DETD(64)

The . . . Fc (Organon Teknika Co., West Chester, Pa., 1.5 .mu.g/ml). As controls, COS cells expressing CD40 were stained with FITC-conjugated G28-5 (**anti-CD40**) or using COS cell supernatants containing sCD72. All incubations were done at room temperature in PBS containing 1 mM CaCl.sub.2,. . .

DETDESC:

DETD(70)

Measurement . . . RPMI medium containing 10% FCS. Reagents used were 1F5 (anti-CD20, 1 .mu.g/ml); PMA (10 ng/ml, LC Services Woburn, Mass.); G28-5 (**anti-CD40**, 1 .mu.g/ml); CD40Ig (5 .mu.g/ml in assays of peripheral blood B cells, 20 .mu.g/ml in assays of tonsilar B cells);. . .

DETDESC:

DETD(75)

To . . . full length CD40 protein (Stamenkovic et al. 1989, EMBO J. 8:1403-1410) and their ability to bind to shgp39, sCD72, and **anti-CD40** mAb examined by fluorescence microscopy. Both the shgp39 and the **anti-CD40** mAb bound to the transfectants while sCD72 did not (FIGS. 3A-3F). In addition, COS cells were transfected with a cDNA. . .

DETDESC:

DETD(84)

The . . . growth and differentiation and the development of antigen-specific B cell lines (Tisch et al., 1988, Immunol. Today 9:145-150). Experiments with **anti-CD40** mAb showed that CD40 signals can synergize with other co-stimulatory signals such as those delivered by anti-CD20 mAb to drive B cell proliferation and that treatment of B cells with **anti-CD40** mAb induces a state of B cell "alertness" which allows them to respond more readily to subsequent activation signals. The. . .

US PAT NO: 5,247,069 [IMAGE AVAILABLE] L5: 2 of 3
INVENTOR: **Jeffrey A. Ledbetter**, Seattle, WA
Edward A. Clark, Seattle, WA

SUMMARY:

BSUM(12)
5.3. Augmentation of B-Cell Proliferation with **Anti-Bp50** Antibody

SUMMARY:

BSUM(13)
5.3.1. **Anti-Bp50** mAb Augments Proliferation Only after B-Cells are Activated by Anti-Bp35 or Anti-u Antibodies

SUMMARY:

BSUM(14)

5.3.2. **Anti-Bp50** mAb do not Activate B-Cells out of G.sub.0 but do Induce Activated B-Cells to Progress Through the Cell Cycle

SUMMARY:

BSUM(15)
5.3.3. Optimal Conditions for Augmenting B-Cell Proliferation with **Anti-Bp50** Antibodies

SUMMARY:

BSUM(16)
5.3.4. Differences Between **Anti-Bp50** and BCGF (Low) Activity

SUMMARY:

BSUM(17)
5.4. Uses of **Anti-Bp50** Ligands and Bp50

SUMMARY:

BSUM(18)
5.4.1. Bp50 Receptor and Uses of Ligands Such as **Anti-Bp50** to Augment B-Cell Proliferation

SUMMARY:

BSUM(32)

The . . . B-cells. Monoclonal antibodies to Bp35, like anti-Ig antibodies, activate tonsillar B-cells and induce low levels of B-cell proliferation. In contrast, **anti-Bp50** monoclonal antibody alone neither activates B-cells nor induces B-cells to proliferate, but together with anti-Bp35 or anti-Ig antibodies, augments B-cell proliferation. In this respect the action of **anti-Bp50** antibody resembles the activity of B-cell growth factors (BCGF). As little as 0.05 ug/ml of **anti-Bp50** is needed to augment proliferation and, like BCGF, **anti-Bp50** is effective even when added 12 to 24 hours after B-cells are activated with anti-Ig or anti-Bp35. Without additional exogenous signals, anti-Bp35 and **anti-Bp50** antibodies together induce strong proliferation of purified resting B-cells. These results suggest that the Bp35 and Bp50 surface molecules function. . .

SUMMARY:

BSUM(33)

Although the activity of **anti-Bp50** resembles that of BCGF (low) since both **anti-Bp50** and BCGF (low) are costimulatory with the same agents but not with each other and both **anti-Bp50** and BCGF (low) affect only activated B-cells and work in a soluble form, the activity of **anti-Bp50** can be distinguished from the activity of BCGF (low), since the proliferation of B-cells stimulated with optimal amounts of **anti-Bp50** and anti-Bp35 (or anti-Ig) can be augmented further with BCGF (low) and both blood B-cells and certain B-cell lymphomas respond differently to **anti-Bp50** versus BCGF. For optimal activity, **anti-Bp50** should be added within 12 hours of B-cell activation, whereas BCGF (low) retains optimal activity even when added 24 hours. . . activation. In addition, Bp50 is expressed on all B-cells while receptors or BCGF (low) are restricted to activated B-cells. Thus **anti-Bp50** and BCGF (low) may coordinately regulate B-cell growth, but apparently do so through distinct signals.

SUMMARY:

BSUM(34)

In . . . can be used to increase an immune response. For example, these ligands which bind Bp50 can be used as an "**adjuvant**" to increase an immune response to a **vaccine**. Alternatively, these ligands can be used to increase the immune response of an immunosuppressed individual.

SUMMARY:

BSUM(57)

FIG. . . . a doubling of fluorescence. The data are presented to show autofluorescent negative cells. PE (red) -anti-Bp35 (1F5) versus FITC (green) -**anti-Bp50** (G28-5) staining shows that all Bp50+ cells are also Bp35+.

SUMMARY:

BSUM(58)

FIG. . . . on 10% SDS polyacrylamide slab gels without reduction. Gels were visualized with autoradiography and intensifying screens. Panel A: lane 1, **anti-Bp50** (G28-5); lane 2, anti-Bp95 (G28-8); lane 3, sepharose-goat anti-mouse Ig only. Exposure time: 4 days. Panel B: lane 1, **anti-Bp50** (G28-5); lane 2, anti-Bp45 (BLAST-2); lane 3, anti-Bp39 (G28-1); lane 4, anti-Bp39 (41-H16); lane 5, sepharose-goat anti-mouse Ig only. An. . .

SUMMARY:

BSUM(59)

FIG. . . . Bp50 expression. Peripheral blood or tonsillar mononuclear cells were isolated by centrifugation on Ficoll and stained with PE (red)-conjugated G28-5 (**anti-Bp50**) in combination with fluorescein (green)-conjugated reference antibodies, including 2C3 (anti-IgM); IF5 (anti-Bp35); HB10a (anti-DR); and 9.6 (anti-CD2, E receptor). Cells. . .

SUMMARY:

BSUM(60)

FIG. 4. Dose response curves for augmentation of proliferation of dense tonsillar Er- B-cells by **anti-Bp50** antibodies as indicated: Media only; **anti-Bp50** only anti-Bp35 (5 ug/ml) only; BCGF only; anti-Bp35 plus BCGF; anti-Bp35 plus graded doses of **anti-Bp50**. Mean proliferation.+-.standard error of quadruplicate samples was measured on day 3.

SUMMARY:

BSUM(61)

FIG. 5. **Anti-Bp50** mAb are most effective at augmenting proliferation if added after a B-cell activation signal. Dense tonsillar Er- B-cells were incubated for 4 days with media only, **anti-Bp50** (0.5 ug/ml) added at different times after incubation, anti-Bp35 (5 ug/ml) added at different times after incubation; **anti-Bp50** kept constant to which anti-Bp35 was added later at different times; anti-Bp35 kept constant to which **anti-Bp50** was added to cultures at different times. During the last 10 hr .sup.3 H-thymidine was added and its incorporation was. . .

SUMMARY:

BSUM(62)

FIG. 6 (A-C). Comparison of the ability of anti-Bp35 and **anti-Bp50** to induce resting tonsillar B-cells to leave the G.sub.0 stage of the cell cycle. Day 3 post treatment media only (.sub.--), anti-Bp35 only (-----); and Ig only (.....), A, no additional additives; B, **anti-Bp50** (0.5 ug/ml) added to each group; C, 5% BCGF added to each group. Data is plotted as relative cell number. . .

SUMMARY:

BSUM(63)

FIG. 7. Kinetics of B-cell proliferation after stimulation with **anti-Bp50** versus BCGF. Dense tonsillar E-B-cells were stimulated with media alone; 10% BCGF only; anti-Bp35 only; **anti-Bp50** only; anti-Bp35+10% BCGF; anti-Bp35 +**anti-Bp50**; and anti-Bp35+anti-Bp50+10% BCGF. Proliferation was measured on the days indicated by an 18-hour pulse of .sup.3 H thymidine. Proliferation was. . .

SUMMARY:

BSUM(64)

FIG. 8 (A and B). Times after anti-Bp35 stimulation when **anti-Bp50** (A) or BCGF (B) optimally augment proliferation. Dense tonsillar E- B-cells were stimulated as shown and proliferation was measured by an 18 hour pulse of 3H thymidine on day 3. Media; anti-Bp35 only added at times indicated; **anti-Bp50** or BCGF only; anti-Bp35 added at start of culture followed by addition of **anti-Bp50** or BCGF at times indicated; **anti-Bp50** or BCGF added at start of culture followed by anti-Bp35. One of two experiments. Proliferation was measured in quadruplicate and standard errors are shown. Doses used: anti-Bp35, 5 ug/ml; **anti-Bp50**, 0.2 ug/nl; BCGF (low) 5%. Concentrations used were as follows: anti-Bp35, 5 ug/ml; **anti-Bp50**, 0.2 ug/ml; BCGF, 5%.

SUMMARY:

BSUM(65)

FIG. 9. **Anti-Bp50** and BCGF have additive effects on B-cell proliferation. Dense tonsillar E- B-cells were stimulated with graded doses of BCGF (low) together with **anti-Bp50** only; anti-Bp35 only; anti-Ig-beads only ; anti-Bp35+**anti-Bp50**; or **anti-Bp50**+anti-Ig. Proliferation was measured on day 3 after stimulation with an 18-hour pulse of .sup.3 H thymidine. Proliferation was measured in quadruplicate and standard errors are shown. One of four experiments. Doses used 10.sup.6 cells anti-Bp35, 5 ug/ml; **anti-Bp50**, 0.2 ug/ml; anti-Ig-beads, 50 ug/ml.

SUMMARY:

BSUM(66)

FIG. 10 (A-D). Comparative effects of **anti-Bp50** and BCGF on normal and malignant B-cells. Peripheral blood E- B-cells (A) or dense tonsillar E- B-cells (C) were stimulated with or without TPA (75 ng/ml) in the presence of 10% BCGF or 1 ug/ml **anti-Bp50**. Two separate B-cell lymphomas (panels B and D) were stimulated in the same way. Proliferation was measured on day 3. . .

SUMMARY:

BSUM(75)

The . . . described which, like BCGF, augments B-cell proliferation. Unlike anti-Bp35 mAb, which can induce resting B-cells in G.sub.0 to enter G.sub.1, **anti-Bp50** mAb does not activate resting B-cells. Anti-Bp35 and **anti-Bp50** mAb together, without any additional exogenous signals, induce strong activation and proliferation of purified B-cells.

SUMMARY:

BSUM(76)

The experiments described below also demonstrate that **anti-Bp50** activity resembles BCGF activity but that antiBp-50 is distinct from one BCGF since **anti-Bp50** and low molecular weight BCGF are clearly additive and act differently on various B-cell subsets or malignancies. Bp50 may be. . .

SUMMARY:

BSUM(91)

The . . . (two color IF) analyses. Using an R-phycoerythrin (PE)-conjugated antibody (red) to the pan B-cell antigen Bp35 (B1, CD20) and fluorescein-conjugated **anti-Bp50** antibody (green), we found that Bp50 was expressed only on Bp35+ B-cells (FIG. 1) in blood or tonsils. Blood B-cells. . .

SUMMARY:

BSUM(92)

The . . . II, eds. Reinherz, et al., Springer Verlag, Berlin, Chap. 12 Vol. 2, 155-167) did not block the binding of fluoresceinated **anti-Bp50** antibodies to B-cells. Thus, based on tissue distribution, biochemical analysis, and blocking studies, the G28-5 monoclonal antibody recognizes a 50-Kd. . .

SUMMARY:

BSUM(96)

5 3. AUGMENTATION OF B-CELL PROLIFERATION WITH **ANTI-Bp50** ANTIBODY

SUMMARY:

BSUM(97)

As . . . Sci. USA 82:1766-1770; Gollay, et al., 1985, J. Immunol. 135:3795-3801). Therefore, it was of interest to compare the effect of **anti-Bp50** mAb in the proliferation of untreated B-cells or B-cells activated with either anti-Bp35 or anti-u antibodies (Table 1). Anti-Bp35 in. . . antibodies attached to Sepharose beads, under appropriate conditions alone, could stimulate some B-cell proliferation (Table 1, line 1); in contrast, **anti-Bp50** antibodies alone did not stimulate proliferation (Table 1, line 2). However, **anti-Bp50** mAb augmented proliferation considerably when cultured with anti-u beads or with anti-Bp35. In this respect **anti-Bp50** resembled BCGF (Table 1, line 3). Thus, it was important to determine whether **anti-Bp50** and BCGF together could induce B-cell proliferation. As illustrated in Table 1, line 4, **anti-Bp50** and BCGF together induced no proliferation, but did augment proliferation of either anti-u

or anti-Bp35 activated cells somewhat more than either stimulant alone. BCGF over a three-log range, when used with **anti-Bp50** without other signals, had no effect on proliferation of dense B-cells even when **anti-Bp50** was used at doses ranging from 0.1 to 10 ug/ml.

SUMMARY:

BSUM(98)

TABLE 1

Augmentation of Anti-Ig or Anti-Bp35 Induced B Cell Proliferation With **Anti-Bp50** Antibodies

Mean Proliferation .+-. S.E. of B Cells Cultured With:

Line	Co-stimulant	Media	Anti-u-beads	Anti-Bp35
1	None	1,212 .+-. 547	10,219 .+-. 462	5,539 .+-. 308
2	**Anti-Bp50**	719 .+-. 718	38,792 .+-. 1,329	25,465 .+-. 616
3	BCGF	456 .+-. 217	14,217 .+-. 445	9,443 .+-. 343
4	**Anti-Bp50** + BCGF	1,456 .+-. 126	54,393 .+-. 2,537	46,488 .+-. 3,387

Proliferation of dense Er tonsillar. . .

SUMMARY:

BSUM(99)

5.3.1. **ANTI-Bp50** mAb AUGMENTS PROLIFERATION ONLY AFTER B-CELLS ARE ACTIVIATED BY ANTI-Bp35 OR ANTI-u-ANTIBODIES

SUMMARY:

BSUM(100)

The results in Table 1 suggest that **anti-Bp50** mAb could not induce proliferation by itself. As shown in FIG. 4, doses of **anti-Bp50** ranging from 0.05 ug to 2.0 ug/ml had no effect on .sup.3 H-thymidine uptake. However, in the presence of optimal levels of anti-Bp35 mAb, as little as 0.1 to 0.5 ug/ml of **anti-Bp50** antibodies augmented proliferation substantially. As much as 50,000 to 70,000 cpm were detectable at the optimal time of proliferation when highly purified B-cells were cultured only with anti-Bp35 plus **anti-Bp50**. A consistent observation was that higher doses of **anti-Bp50** (greater than 2-5 ug/ml) were less effective than doses in the 100-200 ng range.

SUMMARY:

BSUM(101)

These results suggested that **anti-Bp50** may function only after B-cells are activated by other signals. Data shown in FIG. 5 suggest that this is indeed the case. If B-cells were first activated with anti-Bp35, **anti-Bp50** could be added as late as 24-48 hours later and still augment proliferation at day 4. In contrast, when cells were first treated with **anti-Bp50**, anti-Bp35 was effective only if added within a few hours after the start of cultures. Similar results were found when. . .

SUMMARY:

BSUM(102)

5.3.2. **ANTI-Bp50** mAb DO NOT ACTIVATE B-CELLS OUT OF G.sub.0 BUT DO INDUCE ACTIVATED B-CELLS TO PROGRESS THROUGH THE CELL CYCLE

SUMMARY:

BSUM(103)

Previously, . . . the cell cycle (Gollay, et al., 1985, J. Immunol. 135:3795-3801). Thus, it was of interest to compare the ability of **anti-Bp50** mAb to anti-Bp35 mAb for their effects on B-cell activation. As shown in FIG. 6A, unstimulated dense tonsillar B-cells even. . . 15-30% of cells stimulated with anti-Bp35 or anti-u had increased RNA content indicative of entry into G.sub.1. In contrast, neither **anti-Bp50** (FIG. 6B) nor BCGF (FIG. 6C) alone induced significant numbers of B-cells to enter G.sub.1. For instance, 2 days after. . . anti-Bp35 and anti-Ig mAb induced respectively 13.5% and 20.9% of tonsillar cells to enter G.sub.1, whereas cells treated with only **anti-Bp50** (2.7%) or BCGF (3.2%) remained at media control levels (2.2%). However, when either **anti-Bp50** or BCGF were added together with anti-Bp35 or anti-u antibodies, the proportion of cells entering G.sub.1 increased dramatically. Similarly, **anti-Bp50** and BCGF alone did not induce B-cells to enter S phase (Table 2), but together with either anti-Bp35 or anti-u. . .

SUMMARY:

BSUM(104)

TABLE 2

Effect of **Anti-Bp50** and BCGF on Cell Cycle Progression in Tonsillar Lymphocytes Competence

Signal	Progression Signal	% Cells G.sub.0	G.sub.1	S/G.sub.2 /M
media	none	89.9	7.1	2.5
anti-Bp35	"	80.4	14.5	3.7
anti-Ig	"	65.6	27.6	5.7
media	**anti-Bp50**	83.6	12.0	3.3
anti-Bp35	"	54.1	35.5	9.7
anti-Ig	"	43.6	36.2	16.2
media	BCGF	85.4	11.7	2.2
anti-Bp35	". . .			

SUMMARY:

BSUM(105)

5.3.3. OPTIMAL CONDITIONS FOR AUGMENTING B-CELL PROLIFERATION WITH **ANTI-Bp50** ANTIBODIES

SUMMARY:

BSUM(106)

Antibodies . . . resting B-cells (Table 3). However, in the presence of agents that can activate B-cells, such as anti-Ig, anti-Bp35 and TPA, **anti-Bp50** mAb clearly augmented proliferation. **Anti-Bp50** did not costimulate with several interleukins, including purified IL-1, recombinant IL-2 and BCGF (low). A comparison of the effects of **anti-Bp50** with those of BCGF (low) showed that the same agents that were costimulatory with **anti-Bp50** were also costimulatory with BCGF (low) (Table 3). Of particular interest was the finding that together BCGF and **anti-Bp50** still were not costimulatory for resting cells.

SUMMARY:

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=> s (polysaccharide?)(P)(vaccin?)(P)(cytokine?)

        18728 POLYSACCHARIDE?
         8061 VACCIN?
         3301 CYTOKINE?
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L1            0 (POLYSACCHARIDE?)(P)(VACCIN?)(P)(CYTOKINE?)

=> s (polysaccharide?)(P)(adjuvant? or vaccin?)

          18728 POLYSACCHARIDE?
          32634 ADJUVANT?
           8061 VACCIN?
L2          590 (POLYSACCHARIDE?)(P)(ADJUVANT? OR VACCIN?)

=> s l2(P)(b(w)cell or t(w)cell(w)independent)

        1134873 B
         204939 CELL
         515295 T
         204939 CELL
         244254 INDEPENDENT
L3           26 L2(P)(B(W)CELL OR T(W)CELL(W)INDEPENDENT)

=> d l3 1-26
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19. 5,308,838, May 3, 1994, Uses of aloe products; Bill H. McAnalley, et al., 424/278.1; 514/54, 885 [IMAGE AVAILABLE]

20. 5,118,673, Jun. 2, 1992, Uses of aloe products; Robert H. Carpenter, et al., 514/54, 935 [IMAGE AVAILABLE]

21. 5,114,713, May 19, 1992, P. falciparum CS-peptides as universal T-cell epitope; Francesco Sinigaglia, 424/191.1, 268.1, 272.1; 530/324, 326, 350, 806 [IMAGE AVAILABLE]

22. 5,106,616, Apr. 21, 1992, Administration of acemannan; Bill H. McAnalley, et al., 424/85.2; 514/54, 885 [IMAGE AVAILABLE]

23. 4,877,612, Oct. 31, 1989, Immunological adjuvant and process for preparing the same, pharmaceutical compositions, and process; Frank M. Berger, et al., 424/282.1; 514/885, 938, 942 [IMAGE AVAILABLE]

24. 4,590,181, May 20, 1986, Synthetic immunoregulators and methods of use and preparation; Robert E. McCarthy, 424/204.1, 278.1; 514/54; 536/112, 118 [IMAGE AVAILABLE]

25. 4,484,923, Nov. 27, 1984, Method for administering immunopotentiator; Alfred A. Amkraut, et al., 424/85.4, 85.1, 278.1, 282.1; 514/885 [IMAGE AVAILABLE]

26. 4,439,199, Mar. 27, 1984, Method for administering immunopotentiator; Alfred A. Amkraut, et al., 424/278.1, 282.1; 514/885; 530/351 [IMAGE AVAILABLE]

=> d l3 6,12,14 date

L3: 6 of 26

TITLE: Immunogenic conjugate molecules

US PAT NO: 5,681,570 DATE ISSUED: Oct. 28, 1997
[IMAGE AVAILABLE]
APPL-NO: 08/371,965 DATE FILED: Jan. 12, 1995

L3: 12 of 26

TITLE: Dual carrier immunogenic construct
US PAT NO: 5,585,100 DATE ISSUED: Dec. 17, 1996
[IMAGE AVAILABLE]
APPL-NO: 08/402,565 DATE FILED: Mar. 13, 1995
REL-US-DATA: Continuation of Ser. No. 126,017, Sep. 24, 1993, abandoned, which is a continuation of Ser. No. 834,067, Feb. 11, 1992, abandoned.

L3: 14 of 26

TITLE: Synthetic immunoreglators, and methods of use and preparation
US PAT NO: 5,480,642 DATE ISSUED: Jan. 2, 1996
[IMAGE AVAILABLE] DISCL-DATE: May 20, 2003
APPL-NO: 07/224,191 DATE FILED: Jul. 21, 1988
REL-US-DATA: Continuation-in-part of Ser. No. 809,290, Dec. 16, 1985, abandoned, which is a continuation-in-part of Ser. No. 451,016, Dec. 20, 1982, Pat. No. 4,590,181.

=> d l3 6,12,14 kwic

US PAT NO: 5,681,570 [IMAGE AVAILABLE] L3: 6 of 26

SUMMARY:

BSUM(6)

A polyvalent pneumococcus **vaccine** was developed for preventing pneumonia and other invasive diseases due to S. pneumoniae in the adult and aging populations. The **vaccine** contains capsular **polysaccharides** (CPs) from 23 serotypes of S. pneumoniae. These CPs are **T-cell-independent** antigens. They stimulate mainly immunoglobulin M (IgM) antibody with weak memory and readily induce tolerance. Although anticapsular antibodies to S.. . . and immunocompetent individuals, children under 2 years of age and immunocompromised individuals, including the elderly, do not respond well to **T-cell independent** antigens and, therefore, are not afforded optimal protection by the current pneumococcal **vaccines** (ref. 4). There is thus a need to improve the current 23-valent pneumococcus **vaccine**, in order to provide protection for infants and individuals with reduced immuno-responsiveness.

US PAT NO: 5,585,100 [IMAGE AVAILABLE] L3: 12 of 26

SUMMARY:

BSUM(20)

In contrast, T-independent antigens, such as **polysaccharides**, are able to stimulate immune responses in the absence of **adjuvants**. Unfortunately, however, such T-independent antigens cannot stimulate high level or prolonged antibody responses. An even greater disadvantage is their inability to stimulate an immature or **B cell** defective immune system (Mond J. J., Immunological Reviews 64:99, 1982) (Mosier D. E., et al., J. Immunol. 119:1874, 1977). Thus,. . .

US PAT NO: 5,480,642 [IMAGE AVAILABLE] L3: 14 of 26

SUMMARY:

BSUM(4)

A prior art synthetic **adjuvant**, dextran sulfate, has a **polysaccharide** molecule with anionic groups attached. The use of dextran sulfate as an **adjuvant** was disclosed in McCarthy, R. E., Arnold, L. W., and Babcock, G. F.: "Dextran Sulfate: An **Adjuvant** for Cell-Mediated Immune Responses, "Immunology, 32:964, 1977. The immune response was based upon trial and error and it was not known if it would stimulate a T-cell response without a **B-cell** response. It stimulated both T-cell response and **B-cell** response.

=> d l3 1-26 kwic

US PAT NO: 5,721,115 [IMAGE AVAILABLE] L3: 1 of 26

SUMMARY:

BSUM(7)

It . . . will protect individuals against invasive Hib infection, including meningitis. In a randomized, double-blind clinical trial in Finland, a type b **polysaccharide vaccine** was found to be 90% effective in presenting disease in children immunized between 24 and 72 months of age. However, the **vaccine** conferred no protective immunity in children younger than 18 months and provided only limited immunity in children aged 18-23 months. Peltola, et al., N. Engl. J. Med., 310: 1561-1566 (1984). The type b **polysaccharide** elicits a **T-cell-independent** immune response, which probably accounts for the low immunogenicity in young children.

US PAT NO: 5,705,161 [IMAGE AVAILABLE] L3: 2 of 26

SUMMARY:

BSUM(13)

Saccharide . . . a homologous carrier peptide comprising a saccharide part derived from a lipopolysaccharide (LPS) of gram negative bacteria as immunity providing **B cell** activating part. Such a saccharide peptide conjugate offers as advantage the possibility to make a **vaccine** providing immunity against gramnegative bacteria, whose capsular **polysaccharides** provide no or insufficient immune reaction. A saccharide peptide conjugate comprising lipopolysaccharide as immunity providing **B cell** activating part also, however, has disadvantages. Lipopolysaccharide contains toxic parts and a saccharide peptide conjugate comprising a lipopolysaccharide with toxic. . .

US PAT NO: 5,703,060 [IMAGE AVAILABLE] L3: 3 of 26

SUMMARY:

BSUM(25)

Literature which reports that **polysaccharides** possess pharmacological and physiological activities continues to flood the pages of well-respected scientific journals. It is therefore logical that the mucilaginous gel of the Aloe vera plant, which is essentially a **polysaccharide**, holds the secret to Aloe vera's medicinal properties. The controversy over whether the **polysaccharide** is a glucomannan, mannan, pectin, or of some other composition, is resolved by a series of chemical purification steps. Yagi. . . however, earlier isolated pectin as the main component of the same aloe species. As discussed above, the biological activity of **polysaccharides** has been recognized for many years. **Polysaccharide** materials recovered from plants, yeast

and bacteria have demonstrated direct biological activity by eliciting an increase in host defense systems. This reaction is primarily manifested by increased host surveillance for other antigenic substances. **Polysaccharides** serve as **adjuvants** (DEAE Dextran, etc.) and immunomodulators. They also can function as unique **T cell-independent** antigens. Both cellular and humoral immunity may be affected, and increased phagocytosis of infectious organisms and tumor cells has been. . .

US PAT NO: 5,700,787 [IMAGE AVAILABLE] L3: 4 of 26

SUMMARY:

BSUM(21)

According . . . of the pharmaceutical preparations of the invention. Preferred immunomodulators are those that enhance protection against abscess formation. Useful immunomodulators include **adjuvants**; cytokine blockers such as antibodies to tumor necrosis factor, antibodies to interferon and antibodies to interleukin-2 (all of which block. . . immunomodulators and/or antibiotics together with the polymers useful according to the invention as described above. This includes naturally occurring bacterial **polysaccharides** that previously may have been used as immunogens to stimulate a humoral **B cell** response, but have not before been used to protect against abscess formation and have not been used together with immunomodulators and/or antibiotics (e.g. Streptococcus pneumoniae **polysaccharide**, Trypanosoma cruzi lipopeptidophosphoglycan and Pseudomonas aeruginosa Fisher immunotype 7 O-antigen).

US PAT NO: 5,700,649 [IMAGE AVAILABLE] L3: 5 of 26

DETDESC:

DETD(20)

The melanoma tumor cell **vaccine** (MCV) utilizes allogeneic melanoma cell lines which express four well characterized tumor associated antigens, all of which are widely immunogenic. . . IgM response is not consistently translated into an IgG response is not readily apparent. It is probable, however, that the **polysaccharide** moiety of this large glycoprotein molecule induced IgM antibody by **T-cell independent** mechanisms. This would result in the production of low affinity IgM in small quantities without a subsequent switch to IgG. . .

US PAT NO: 5,681,570 [IMAGE AVAILABLE] L3: 6 of 26

SUMMARY:

BSUM(6)

A polyvalent pneumococcus **vaccine** was developed for preventing pneumonia and other invasive diseases due to S. pneumoniae in the adult and aging populations. The **vaccine** contains capsular **polysaccharides** (CPs) from 23 serotypes of S. pneumoniae. These CPs are **T-cell-independent** antigens. They stimulate mainly immunoglobulin M (IgM) antibody with weak memory and readily induce tolerance. Although anticapsular antibodies to S.. . . and immunocompetent individuals, children under 2 years of age and immunocompromised individuals, including the elderly, do not respond well to **T-cell independent** antigens and, therefore, are not afforded optimal protection by the current pneumococcal **vaccines** (ref. 4). There is thus a need to improve the current 23-valent pneumococcus **vaccine**, in order to provide protection for infants and

individuals with reduced immuno-responsiveness.

US PAT NO: 5,679,547 [IMAGE AVAILABLE] L3: 7 of 26

SUMMARY:

BSUM(6)

It . . . will protect individuals against invasive Hib infection, including meningitis. In a randomized, double-blind clinical trial in Finland, a type b **polysaccharide vaccine** was found to be 90% effective in presenting disease in children immunized between 24 and 72 months of age. However, the **vaccine** conferred no protective immunity in children younger than 18 months and provided only limited immunity in children aged 18-23 months. Peltola, et al., N. Engl. J. Med., 310:1561-1566 (1984). The type b **polysaccharide** elicits a **T-cell-independent** immune response, which probably accounts for the low immunogenicity in young children.

US PAT NO: 5,668,272 [IMAGE AVAILABLE] L3: 8 of 26

DETDESC:

DETD(57)

Neoglycopeptides . . . et al J Med Chem 24:1388;1981; Fendersen, B. A. et al J Exp Med 160:1591;1984) for the development of synthetic **vaccines** against tumors (Toyokuni, T. et al Tetrahedron Lett 31:2673;1990). Conjugation of **polysaccharides** (which are often **T-cell independent**) to protein carriers has been used to convert them into T-cell dependent antigens with enhanced immunogenicity, which have the potential to be **vaccine** candidates (Jennings, H. J. Adv Carb Chem Biochem 41:155;1983).

US PAT NO: 5,648,241 [IMAGE AVAILABLE] L3: 9 of 26

DETDESC:

DETD(6)

Differences in immunogenicity have also been observed with the capsular **polysaccharides** of other bacteria. For example, the **vaccine** against the type C meningococcal capsule is highly active while the group B meningococcal **polysaccharide vaccine** is not immunogenic (Kasper, D. L, et al., J. Infec. Dis. 153:407-415 (1986)). **T-cell independent** functions of the host's immune system are often required for mounting an antibody response to **polysaccharide** antigens. The lack of a **T-cell independent** response to **polysaccharide** antigens may be responsible for the low levels of antibody against group B Streptococcus present in mothers whose children subsequently. . . B Streptococcus. In addition, children prior to 18 or 24 months of age have a poorly developed immune response to **T-cell independent** antigens.

DETDESC:

DETD(21)

The present invention surmounts the above-discussed deficiencies of prior **vaccines** to group B Streptococcus through the development of a conjugate **vaccine** in which the capsular **polysaccharides** are covalently linked to a protein backbone. This approach supports the development of a T-cell dependent antibody response to the capsular **polysaccharide** antigens and circumvents the **T-cell independent** requirements for antibody production (Baker, C. J, et

al., Rev. of Infec. Dis. 7:458-467 (1985), Kasper, D. L. et al.,. . .

US PAT NO: 5,623,057 [IMAGE AVAILABLE] L3: 10 of 26

SUMMARY:

BSUM(3)

Polyvalent **vaccines** have been produced that are efficacious in raising protective immune responses against the pneumococci in adults. "PNEUMOVAX.RTM. 23" (Pneumococcal **Vaccine** Polyvalent, MSD; see PDR, 1990 edition, p. 1431), for example, is a liquid composition containing 50 .mu.g/ml of each of the 23 different, unconjugated pneumococcal **polysaccharides**, all of which are on deposit with the ATCC and provid one possible source of starting material for this invention. "PNEUMOVAX.RTM. 23" comprises each of the following free, that is unconjugated, **polysaccharides**: 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F and 33F, accounting for about 90% of pneumococcal blood isolates. However, such **vaccines** are least effective in the segment of the population most at risk for pneumococcal infections: **B-Cell** immunocompromised individuals, the elderly and infants younger than two years old who depend on T-cell responses for immune protection. Since unconjugated **polysaccharides** are poor inducers of T-cell immune responses, conversion of the Pn-Ps into immunogens capable of inducing T-cell responses is the. . . protection in this target population. Use, however, is not restricted to this group of individuals. For example, administration of a **vaccine**, comprising one or more of the novel conjugates, to a female mammal prior to or during pregnancy raises antibodies in the mother which can passively protect a developing fetus and suckling infant even though the **vaccine** is not administered directly to the fetus or infant. Such conjugate **vaccines** should also prove useful for eliciting antibodies for ultimate passive protection of at risk populations, such as newborns or siblings. . .

SUMMARY:

BSUM(12)

It is an object of this invention to provide novel, partially-hydrolyzed and highly purified antigenically type-specific pneumococcal capsular **polysaccharides** (Pn-Ps), useful as intermediates in the preparation of T-cell dependent conjugates of the Pn-Ps and immunogenic proteins. Another object is to provide T-cell dependent conjugates of the Pn-Ps and immunogenic proteins, useful in **vaccine** compositions to prevent pneumococcal infections, especially in infants younger than two years old and in **B-cell** immunocompromised people. Another object is to provide a process, improved over that provided in U.S. Pat. No. 4,695,624, for the formation of covalent pneumococcal **polysaccharide**-immunogenic protein conjugates (Pn-Ps-Pro), wherein the improvement consists of greater chemical definition and purity of the starting Pn-Ps, intermediates, final product. . . and in immunocompromised individuals. Another object is to provide a method of treatment, employing these conjugates in immunologically-effective amounts in **vaccine** formulations, to prevent pneumococcal induced diseases such as otitis media, meningitis, pneumonia, bacteremia and the acute exacerbations of chronic arthritis,. . .

US PAT NO: 5,587,364 [IMAGE AVAILABLE] L3: 11 of 26

SUMMARY:

BSUM(25)

Literature which reports that **polysaccharides** possess

pharmacological and physiological activities continues to flood the pages of well-respected scientific journals. It is therefore logical that the mucilaginous gel of the Aloe vera plant, which is essentially a **polysaccharide**, holds the secret to Aloe vera's medicinal properties. The controversy over whether the **polysaccharide** is a glucomannan, mannan, pectin, or of some other composition, is resolved by a series of chemical purification steps. Yagi. . . however, earlier isolated pectin as the main component of the same aloe species. As discussed above, the biological activity of **polysaccharides** has been recognized for many years. **Polysaccharide** materials recovered from plants, yeast and bacteria have demonstrated direct biological activity by eliciting an increase in host defense systems. This reaction is primarily manifested by increased host surveillance for other antigenie substances. **Polysaccharides** serve as **adjuvants** (DEAE Dextran, etc.) and immunomodulators. They also can function as unique **T cell-independent** antigens. Both cellular and humoral immunity may be affected, and increased phagocytosis of infectious organisms and tumor cells has been. . .

US PAT NO: 5,585,100 [IMAGE AVAILABLE] L3: 12 of 26

SUMMARY:

BSUM(20)

In contrast, T-independent antigens, such as **polysaccharides**, are able to stimulate immune responses in the absence of **adjuvants**. Unfortunately, however, such T-independent antigens cannot stimulate high level or prolonged antibody responses. An even greater disadvantage is their inability to stimulate an immature or **B cell** defective immune system (Mond J. J., Immunological Reviews 64:99, 1982) (Mosier D. E., et al., J. Immunol. 119:1874, 1977). Thus,. . .

US PAT NO: 5,518,725 [IMAGE AVAILABLE] L3: 13 of 26

SUMMARY:

BSUM(19)

Most . . . have been made to reduce the quantity of Ag needed to produce the desired response. In one approach, a mucosal **adjuvant** is administered together with the immunogen for which a mucosal response is desired. For example, M. Vadjy et al. (1992).. . . ("KLH") in the intestinal lamina propria of mice by oral priming immunizations with KLH in combination with cholera toxin ("CT") **adjuvant**. The induced memory responses to KLH in the gut were not reflected in changes in KLH-specific antibody (Ab) titres in. . . experiments. CT is a known highly potent mucosal immunogen that additionally has an ability to act as a strong mucosal **adjuvant** to related as well as unrelated antigens; it also is exceedingly toxic. E. Abraham et al. (1992). Jour. Immunol. 149: 3719-26, describes obtaining substantial enhancement of bacterial **polysaccharide**-specific sIgA response in the lungs of mice, by intranasally administering liposomes containing interleukin-2 ("IL-2"), a cytokine known to augment **B cell** proliferation and progression to immunoglobulin ("Ig") production, together with bacterial **polysaccharide** from Pseudomonas aeruginosa or Aerobacter levanicum; and an enhancement in those mice of resistance to infection. In contrast, there were no significant changes in bacterial **polysaccharide**-specific Ig in the serum of the mice immunized with liposomes containing both IL-2 and P. aeruginosa bacterial **polysaccharide**. Encapsulation of IL-2 in liposomes was thought to avoid the toxicity that results from high systemic levels of this cytokine.

US PAT NO: 5,480,642 [IMAGE AVAILABLE] L3: 14 of 26

SUMMARY:

BSUM(4)

A prior art synthetic **adjuvant**, dextran sulfate, has a **polysaccharide** molecule with anionic groups attached. The use of dextran sulfate as an **adjuvant** was disclosed in McCarthy, R. E., Arnold, L. W., and Babcock, G. F.: "Dextran Sulfate: An **Adjuvant** for Cell-Mediated Immune Responses, "Immunology, 32:964, 1977. The immune response was based upon trial and error and it was not known if it would stimulate a T-cell response without a **B-cell** response. It stimulated both T-cell response and **B-cell** response.

US PAT NO: 5,474,905 [IMAGE AVAILABLE] L3: 15 of 26

SUMMARY:

BSUM(9)

First, . . . 84 known different serotypes of Streptococcus pneumoniae and each serotype has a unique capsular structure. Thus, immunization with purified capsular **polysaccharides** for 23 of the most common strains of Streptococcus pneumoniae only prevents the subsequent infection by those specific pneumococcal serotypes. Therefore, an individual **vaccinated** by the current **vaccine** would not be protected from a majority of the known serotypes of Streptococcus pneumoniae that cause a variety of diseases. Field studies have shown that the 23-valent capsular **vaccine** provides protection against the **vaccine**-type pneumococcal infection 65% of the time and only protects against all serotypes 0-60% of the time. Second, **polysaccharides** are not good antigens; especially those isolated from serotypes 6 and 14 of Streptococcus pneumoniae, which are major pathogens in pediatric otitis media and meningitis. Third, the antibody production elicited by **polysaccharide** is **T-cell independent** and cannot be enhanced by a second immunization. Forth, the immune response to the current **vaccine** in the elderly and children under two years of age is weak and cannot protect them against pneumococcal infection.

SUMMARY:

BSUM(12)

The present invention solves the problems associated with the present antibiotic and **vaccine** therapies for pneumococcal diseases (i.e., diseases caused by Streptococcus pneumoniae). The present invention is directed, inter alia, to isolated hemin/hemoglobin-binding. . . 66 and 76 kDa, respectively, which are immunogenic and highly conserved among all serotypes of Streptococcus pneumoniae. Unlike the capsular **polysaccharides** of the 23 strains of Streptococcus pneumoniae described in the prior art, the hemin/hemoglobin-binding proteins described in this invention can serve as antigens for most, if not all, pneumococcal serotypes, are not **T-cell independent** and are prophylactic against pneumococcal infection. A preferred embodiment of this invention is the isolated hemin/hemoglobin-binding protein of Streptococcus pneumoniae. . . art. The present invention provides antibodies to these antigens and compositions containing these antigens. The present invention also provides new **vaccines** and diagnostic methods including kits to both diagnose and treat human pneumococcal infections.

US PAT NO: 5,468,737 [IMAGE AVAILABLE] L3: 16 of 26

SUMMARY:

BSUM(34)

As discussed above, the biological activities of **polysaccharide** materials recovered from plants, yeast and bacteria have demonstrated direct biological activities by eliciting an increase in host defense systems. This reaction is primarily manifested by increased host surveillance for other antigenic substances. **Polysaccharides** serve as **adjuvants** (DEAE, Dextran, etc.) and immunomodulators. They also can function as unique **T-cell-independent** antigens. Both cellular and humoral immunity may be affected, and increased phagocytosis of infectious organisms and tumor cells has been. . .

US PAT NO: 5,441,943 [IMAGE AVAILABLE] L3: 17 of 26

SUMMARY:

BSUM(25)

Literature which reports that **polysaccharides** possess pharmacological and physiological activities continues to flood the pages of well-respected scientific journals. It is therefore logical that the mucilaginous gel of the Aloe vera plant, which is essentially a **polysaccharide**, holds the secret to Aloe vera's medicinal properties. The controversy over whether the **polysaccharide** is a glucomannan, mannan, pectin, or of some other composition, is resolved by a series of chemical purification steps. Yagi. . . however, earlier isolated pectin as the main component of the same aloe species. As discussed above, the biological activity of **polysaccharides** has been recognized for many years. **Polysaccharide** materials recovered from plants, yeast and bacteria have demonstrated direct biological activity by eliciting an increase in host defense systems. This reaction is primarily manifested by increased host surveillance for other antigenic substances. Polysacchardies serve as **adjuvants** (DEAE Dextran, etc.) and immunomodulators. They also can function as unique **T cell-independent** antigens. Both cellular and humoral immunity may be affected, and increased phagocytosis of infectious organisms and tumor cells has been. . .

US PAT NO: 5,409,703 [IMAGE AVAILABLE] L3: 18 of 26

SUMMARY:

BSUM(36)

As discussed above, the biological activities of **polysaccharide** materials recovered from plants, yeast and bacteria have demonstrated direct biological activities by eliciting an increase in host defense systems. This reaction is primarily manifested by increased host surveillance for other antigenic substances. **Polysaccharides** serve as **adjuvants** (DEAE, Dextran, etc.) and immunomodulators. They also can function as unique **T-cell-independent** antigens. Both cellular and humoral immunity may be affected, and increased phagocytosis of infectious organisms and tumor cells has been. . .

US PAT NO: 5,308,838 [IMAGE AVAILABLE] L3: 19 of 26

SUMMARY:

BSUM(25)

Literature which reports that **polysaccharides** possess pharmacological and physiological activities continues to flood the pages of well-respected scientific journals. It is therefore logical that the mucilaginous gel of the Aloe vera plant, which is essentially a **polysaccharide**, holds the secret to Aloe vera's medicinal properties. The controversy over whether the **polysaccharide** is a glucomannan,

mannan, pectin, or of some other composition, is resolved by a series of chemical purification steps. Yagi. . . however, earlier isolated pectin was the main component of the same aloe species. As discussed above, the biological activity of **polysaccharides** has been recognized for many years. **Polysaccharide** materials recovered from plants, yeast and bacteria have demonstrated direct biological activity by eliciting an increase in host defense systems. This reaction is primarily manifested by increased host surveillance for other antigenic substances. **Polysaccharides** serve as **adjuvants** (DEAE Dextran, etc.) and immunomodulators. They also can function as unique **T cell-independent** antigens. Both cellular and humoral immunity may be affected, and increased phagocytosis of infectious organisms and tumor cells has been. . .

US PAT NO: 5,118,673 [IMAGE AVAILABLE] L3: 20 of 26

SUMMARY:

BSUM(25)

Literature which reports that **polysaccharides** possess pharmacological and physiological activities continues to flood the pages of well-respected scientific journals. It is therefore logical that the mucilaginous gel of the Aloe vera plant, which is essentially a **polysaccharide**, holds the secret to Aloe vera's medicinal properties. The controversy over whether the **polysaccharide** is a glucomannan, mannan, pectin, or of some other composition, is resolved by a series of chemical purification steps. Yagi. . . however, earlier isolated pectin was the main component of the same aloe species. As discussed above, the biological activity of **polysaccharides** has been recognized for many years. **Polysaccharide** materials recovered from plants, yeast and bacteria have demonstrated direct biological activity by eliciting an increase in host defense systems. This reaction is primarily manifested by increased host surveillance for other antigenic substances. **Polysaccharides** serve as **adjuvants** (DEAE Dextran, etc.) and immunomodulators. They also can function as unique **T cell-independent** antigens. Both cellular and humoral immunity may be affected, and increased phagocytosis of infectious organisms and tumor cells has been. . .

US PAT NO: 5,114,713 [IMAGE AVAILABLE] L3: 21 of 26

SUMMARY:

BSUM(31)

The immunogenic compositions comprising a peptide representing a universal T-cell epitope according to the present invention and a peptide representing a **B-cell** epitope may comprise additionally a pharmaceutically acceptable **adjuvant**. The said immunogenic compositions can be used as **vaccines** to elicit the formation of antibodies specific for a pathogenic agent expressing the **B-cell** epitope mentioned above. The term "Pharmaceutically acceptable **adjuvant**" can mean either the standard compositions which are suitable for human administration or the typical **adjuvants** and excipients (e.g. serum albumin or plasma preparations) employed in animal **vaccinations**. Suitable **adjuvants** for the **vaccination** of animals include but are not limited to Freund's complete or incomplete **adjuvant** (not suitable for human or livestock use). **Adjuvant** 65 (containing peanut oil, mannide monooleate and aluminum monostearate), mineral gels such as aluminum hydroxide, aluminum phosphate and alum. surfactants. . . polypeptide of the present invention can also be administered following incorporation into liposomes or other micro-carriers, or after conjugation to **polysaccharides**, other proteins or other polymers or in combination with Quil-A to form "Iscoms"

(immunostimulating complexes) (Allison et al., J. Immunol. Meth. 95, 157-168 [1986]; Morein et al., Nature 308, 457-460 [1984]). In addition, genetically engineered microorganisms such as **vaccinia** or salmonella which are capable of expressing genes encoding a polypeptide representing a universal T-cell epitope can be used as **vaccine** delivery systems (Mackett. Immunol. Letters 16, 243-248 [1987]).

US PAT NO: 5,106,616 [IMAGE AVAILABLE] L3: 22 of 26

SUMMARY:

BSUM(25)

As discussed above, the biological activity of **polysaccharides** has been recognized for many years. **Polysaccharide** materials recovered from plants, yeast and bacteria have demonstrated direct biological activity by eliciting an increase in host defense systems. This reaction is primarily manifested by increased host surveillance for other antigenic substances. **Polysaccharides** serve as **adjuvants** (Freund's, etc.) and immunomodulators. They also function as unique **T cell-independent** antigens. Both cellular and humoral immunity may be affected, and increased phagocytosis of infectious organisms and tumor cells has been. . .

US PAT NO: 4,877,612 [IMAGE AVAILABLE] L3: 23 of 26

DETDESC:

DETD(27)

It is well recognized that **polysaccharides** are much poorer immunogens than protein antigens. This has been a problem, particularly in the preparation of **vaccines** for the prevention of infections by N. meningitidis, H. influenzae and S. pneumoniae. The problem with development of these **vaccines** is particularly acute in infants who do not form antibodies to these **vaccines** during the first 18 months of their lives. It has now been determined that infants have a natural ontogenic delay in the formation of **B-cell** populations, responding to **polysaccharide** antigen TI2, and that this is the cause of the high incidence o meningitis produced by N. meningitidis and H.. . .

US PAT NO: 4,590,181 [IMAGE AVAILABLE] L3: 24 of 26

SUMMARY:

BSUM(4)

A prior art synthetic **adjuvant**, dextran sulfate, has a **polysaccharide** molecule with anionic groups attached. The use of dextran sulfate as an **adjuvant** was disclosed in McCarthy, R. E., Arnold, L. W., and Babcock, G. F.: "Dextran Sulfate: An **Adjuvant** for Cell-Mediated Immune Responses," Immunology, 32:963, 1977. The immune response is based upon trial and error and it was not known if it would stimulate a T-cell response without a **B-cell** response.

US PAT NO: 4,484,923 [IMAGE AVAILABLE] L3: 25 of 26

SUMMARY:

BSUM(24)

The . . . polyribonucleotides, and glucan; improves T cell responses by administering a member selected from the group consisting of levamisole, BCG-Freund's complete **adjuvant**, and B. pertussis;

increase in **B cell** responses by administering a member selected from the group consisting of pyran, glucan, C. parvum, B. pertussis, endotoxins, Bordetella, mycobacterium, retinol BCG-Freund's **adjuvant**, and tilorone; increase in complement activity by administering levamisole or zymosan; and induce interferon production by administering a member selected from the group consisting of pyran, endotoxin, **polysaccharides**, poly I:C, other polycations, and tilorone. The potentiating effects of immunostimulants are known in the Fundamentals of Clinical Immunology, by. . .

US PAT NO: 4,439,199 [IMAGE AVAILABLE] L3: 26 of 26

SUMMARY:

BSUM(24)

The . . . polyribonucleotides, and glucan; improves T cell responses by administering a member selected from the group consisting of levamisole, BCG-Freund's complete **adjuvant**, and B. pertussis; increase in **B cell** responses by administering a member selected from the group consisting of pyran, glucan, C. parvum, B. pertussis, endotoxins, Bordetella, mycobacterium, retinol BCG-Freund's **adjuvant**, and tilorone; increase in complement activity by administering levamisole or zymosan; and induce interferon production by administering a member selected from the group consisting of pyran, endotoxin, **polysaccharides**, poly I:C, other polycations, and tilorone. The potentiating effects of immunostimulants are known in the Fundamentals of Clinical Immunology, by. . .

```
=> s (t(w)cell(w)independent)(P)(adjuvant? or vaccin?)

        515295 T
        204939 CELL
        244254 INDEPENDENT
         32634 ADJUVANT?
          8061 VACCIN?
L4          34 (T(W)CELL(W)INDEPENDENT)(P)(ADJUVANT? OR VACCIN?)

=> d l4 1-34
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1. 5,738,855, Apr. 14, 1998, Synthesis of typhoid fever vaccine from a plant or fruit polysaccharide; Shousun Chen Szu, et al., 424/258.1, 184.1, 192.1, 197.1, 236.1; 514/2, 53; 530/402; 536/123 [IMAGE AVAILABLE]

2. 5,721,115, Feb. 24, 1998, DNA encoding a novel Haemophilus influenzae protein; Howard C. Krivan, et al., 435/69.1; 424/200.1, 256.1; 435/69.3, 320.1; 530/350; 536/23.1, 23.7 [IMAGE AVAILABLE]

3. 5,703,060, Dec. 30, 1997, Uses of aloe products in the prevention and treatment of infections and infestations; Bill H. McAnalley, et al., 514/54, 885 [IMAGE AVAILABLE]

4. 5,700,649, Dec. 23, 1997, Method of detection of urinary tumor associated antigen; Donald L. Morton, et al., 435/7.1; 424/141.1, 142.1, 277.1; 435/7.9, 7.92, 7.93, 7.94; 436/507, 536 [IMAGE AVAILABLE]

5. 5,681,570, Oct. 28, 1997, Immunogenic conjugate molecules; Yan-ping Yang, et al., 424/197.11, 203.1, 234.1, 244.1, 256.1; 514/54; 536/123.1 [IMAGE AVAILABLE]

6. 5,679,547, Oct. 21, 1997, Method for producing a novel purified Haemophilus influenzae protein; Howard C. Krivan, et al., 435/69.3; 424/256.1; 435/7.1, 69.1, 172.3; 530/350, 412 [IMAGE AVAILABLE]

7. 5,668,272, Sep. 16, 1997, Method for producing synthetic N-linked glycoconjugates; A. V. Krishna Prasad, et al., 536/55.3; 530/322; 536/55.2 [IMAGE AVAILABLE]

8. 5,653,977, Aug. 5, 1997, Anti-idiotypic antibody that mimics the GD2 antigen; Mansoor N. Saleh, 424/131.1, 137.1, 138.1, 142.1; 435/327, 329, 330, 344.1; 530/387.2, 387.5, 387.7, 388.15 [IMAGE AVAILABLE]

9. 5,648,241, Jul. 15, 1997, Conjugate vaccine against group B streptococcus; James L. Michel, et al., 435/69.3, 252.33, 253.4, 320.1; 536/23.7 [IMAGE AVAILABLE]

10. 5,587,364, Dec. 24, 1996, Uses of aloe products in the treatment of inflammatory diseases; Bill H. McAnalley, et al., 514/54, 885, 886; 536/123.1 [IMAGE AVAILABLE]

11. 5,476,784, Dec. 19, 1995, Gonococcal anti-idiotypic antibodies and methods and compositions using them; Peter A. Rice, et al., 435/327, 7.32, 70.2, 172.2; 530/387.2, 387.5, 388.2, 388.4 [IMAGE AVAILABLE]

12. 5,474,905, Dec. 12, 1995, Antibodies specific for streptococcus pneumoniae hemin/hemoglobin-binding antigens; Stanley S. Tai, et al.,

435/7.34, 885, 975; 436/548; 530/388.4, 389.5 [IMAGE AVAILABLE]

13. 5,468,737, Nov. 21, 1995, Wound healing accelerated by systemic administration of polysaccharide from aloe; Bill H. McAnalley, et al., 514/54; 424/74, 195.1, 423, 615; 514/25, 458; 536/123, 124 [IMAGE AVAILABLE]

14. 5,441,943, Aug. 15, 1995, Uses of aloe products; Bill H. McAnalley, et al., 514/54, 824; 536/123.1 [IMAGE AVAILABLE]

15. 5,441,942, Aug. 15, 1995, 2'3'-dideoxy-2',3'-didehydro-7,8-disubstituted guanosines and their immunostimulative effect; Michael G. Goodman, et al., 514/45; 536/27.14, 27.81 [IMAGE AVAILABLE]

16. 5,439,907, Aug. 8, 1995, Use of N9 morpholino derivatives of 7,8-disubstituted guanines; Robert Chen, et al., 514/234.2; 435/375 [IMAGE AVAILABLE]

17. 5,409,703, Apr. 25, 1995, Dried hydrogel from hydrophilic-hygroscopic polymer; Bill H. McAnalley, et al., 424/435, 78.06, 78.08, 93.6, 195.1, 423, 443; 536/128 [IMAGE AVAILABLE]

18. 5,382,580, Jan. 17, 1995, N9 morpholino derivatives of 7,8-disubstituted guanines; Robert Chen, et al., 514/234.2; 544/118 [IMAGE AVAILABLE]

19. 5,370,871, Dec. 6, 1994, Therapeutic suppression of specific immune responses by administration of oligomeric forms of antigen of controlled chemistry; Howard M. Dintzis, et al., 424/244.1, 184.1; 514/2, 23, 25; 530/412, 413, 807; 536/123.1 [IMAGE AVAILABLE]

20. 5,317,013, May 31, 1994, Modulation of animal cellular responses with compositions containing 8-substituted guanine derivatives; Michael G. Goodman, et al., 514/45; 424/85.2; 514/885; 530/351 [IMAGE AVAILABLE]

21. 5,308,838, May 3, 1994, Uses of aloe products; Bill H. McAnalley, et al., 424/278.1; 514/54, 885 [IMAGE AVAILABLE]

22. 5,166,141, Nov. 24, 1992, Immunostimulating 7-deaza-7-oxa- and 7-deaza-7-oxo-analogs of 8-substituted-guanine-9-(1'-beta-D-aldoglycosidyl) derivatives and methods of treating test animals; Michael G. Goodman, et al., 514/45; 544/255 [IMAGE AVAILABLE]

23. 5,147,636, Sep. 15, 1992, Modulation of animal cellular responses with compositions containing 8-substituted guanine derivatives and interferons; Michael G. Goodman, et al., 424/85.4, 85.5, 85.6, 85.7 [IMAGE AVAILABLE]

24. 5,126,131, Jun. 30, 1992, Therapeutic suppression of specific immune responses by administration of antigen-competitive conjugates.; Howard M. Dintzis, et al., 424/193.1, 184.1, 810; 514/2, 8, 10, 21; 530/402, 403, 404, 405, 406, 807, 810, 813 [IMAGE AVAILABLE]

25. 5,118,673, Jun. 2, 1992, Uses of aloe products; Robert H. Carpenter, et al., 514/54, 935 [IMAGE AVAILABLE]

26. 5,106,616, Apr. 21, 1992, Administration of acemannan; Bill H. McAnalley, et al., 424/85.2; 514/54, 885 [IMAGE AVAILABLE]

27. 5,102,663, Apr. 7, 1992, Vaccine for stimulating or enhancing production of antibodies against 9-O-acetyl GD3; Philip O. Livingston, et al., 424/277.1, 137.1, 184.1, 422, 423; 436/23, 503, 813, 822, 823; 514/25, 885; 530/387.5, 389.7, 806, 842 [IMAGE AVAILABLE]

28. 4,948,730, Aug. 14, 1990, Modulation of animal cellular responses

with compositions containing 8-substituted guanine derivatives; Michael G. Goodman, et al., 435/70.5; 424/85.4 [IMAGE AVAILABLE]

29. 4,900,675, Feb. 13, 1990, Modulation of animal cellular responses with compositions containing isoxanthopterin-8-(1'-.beta.-aldoglycosidyl) derivatives; Michael G. Goodman, 514/43, 45 [IMAGE AVAILABLE]

30. 4,894,229, Jan. 16, 1990, Carrier-bound immunogenic determinants and carrier therefor; Alfred Polson, et al., 424/130.1, 194.1, 197.11, 804; 435/131, 132, 137, 176, 177, 181, 252.1, 252.8, 820; 514/2, 21, 885; 530/810 [IMAGE AVAILABLE]

31. 4,849,411, Jul. 18, 1989, Modulation of animal cellular responses with compositions containing 8-substituted guanine derivatives; Michael G. Goodman, et al., 514/45; 424/278.1; 435/375 [IMAGE AVAILABLE]

32. 4,762,713, Aug. 9, 1988, Boosting of immunogenic conjugate vaccinations by unconjugated bacterial capsular polymers; Porter W. Anderson, 424/197.11, 236.1, 237.1, 238.1, 239.1, 240.1, 250.1, 256.1, 257.1, 260.1, 831, 832 [IMAGE AVAILABLE]

33. 4,643,992, Feb. 17, 1987, Modulation of animal cellular responses with compositions containing 8-substituted guanine derivatives; Michael G. Goodman, et al., 514/45 [IMAGE AVAILABLE]

34. 4,539,205, Sep. 3, 1985, Modulation of animal cellular responses with compositions containing 8-substituted guanine derivatives; Michael G. Goodman, et al., 514/45; 424/85.1 [IMAGE AVAILABLE]

=> d l4 1-34 kwic

US PAT NO: 5,738,855 [IMAGE AVAILABLE] L4: 1 of 34

SUMMARY:

BSUM(5)

The immunologic properties of the Vi that limits its use as a **vaccine** are: 1) only .about.70% efficacy in individuals 5 to 45 years of age; 2) an age-dependent serum antibody response, Vi. . . . levels of antibodies in a fraction of children <2 years-old and; 3) reinjection did not elicit a booster antibody response (**T-cell independent**) [15,19]. To increase its immunogenicity and to induce T-cell dependence, the Vi was conjugated to proteins [22,24,25]. A clinical trial. . .

US PAT NO: 5,721,115 [IMAGE AVAILABLE] L4: 2 of 34

SUMMARY:

BSUM(7)

It . . . protect individuals against invasive Hib infection, including meningitis. In a randomized, double-blind clinical trial in Finland, a type b polysaccharide **vaccine** was found to be 90% effective in presenting disease in children immunized between 24 and 72 months of age. However, the **vaccine** conferred no protective immunity in children younger than 18 months and provided only limited immunity in children aged 18-23 months. Peltola, et al., N. Engl. J. Med., 310: 1561-1566 (1984). The type b polysaccharide elicits a **T-cell-independent** immune response, which probably accounts for the low immunogenicity in young children.

US PAT NO: 5,703,060 [IMAGE AVAILABLE] L4: 3 of 34

SUMMARY:

BSUM(25)

Literature . . . in host defense systems. This reaction is primarily manifested by increased host surveillance for other antigenic substances. Polysaccharides serve as **adjuvants** (DEAE Dextran, etc.) and immunomodulators. They also can function as unique **T cell-independent** antigens. Both cellular and humoral immunity may be affected, and increased phagocytosis of infectious organisms and tumor cells has been. . .

US PAT NO: 5,700,649 [IMAGE AVAILABLE] L4: 4 of 34

DETDESC:

DETD(20)

The melanoma tumor cell **vaccine** (MCV) utilizes allogeneic melanoma cell lines which express four well characterized tumor associated antigens, all of which are widely immunogenic. . . not readily apparent. It is probable, however, that the polysaccharide moiety of this large glycoprotein molecule induced IgM antibody by **T-cell independent** mechanisms. This would result in the production of low affinity IgM in small quantities without a subsequent switch to IgG. . .

US PAT NO: 5,681,570 [IMAGE AVAILABLE] L4: 5 of 34

SUMMARY:

BSUM(6)

A polyvalent pneumococcus **vaccine** was developed for preventing pneumonia and other invasive diseases due to S. pneumoniae in the adult and aging populations. The **vaccine** contains capsular polysaccharides (CPs) from 23 serotypes of S. pneumoniae. These CPs are **T-cell-independent** antigens. They stimulate mainly immunoglobulin M (IgM) antibody with weak memory and readily induce tolerance. Although anticapsular antibodies to S.. . . and immunocompetent individuals, children under 2 years of age and immunocompromised individuals, including the elderly, do not respond well to **T-cell independent** antigens and, therefore, are not afforded optimal protection by the current pneumococcal **vaccines** (ref. 4). There is thus a need to improve the current 23-valent pneumococcus **vaccine**, in order to provide protection for infants and individuals with reduced immuno-responsiveness.

US PAT NO: 5,679,547 [IMAGE AVAILABLE] L4: 6 of 34

SUMMARY:

BSUM(6)

It . . . protect individuals against invasive Hib infection, including meningitis. In a randomized, double-blind clinical trial in Finland, a type b polysaccharide **vaccine** was found to be 90% effective in presenting disease in children immunized between 24 and 72 months of age. However, the **vaccine** conferred no protective immunity in children younger than 18 months and provided only limited immunity in children aged 18-23 months. Peltola, et al., N. Engl. J. Med., 310:1561-1566 (1984). The type b polysaccharide elicits a **T-cell-independent** immune response, which probably accounts for the low immunogenicity in young children.

US PAT NO: 5,668,272 [IMAGE AVAILABLE] L4: 7 of 34

DETDESC:

DETD(57)

Neoglycopeptides . . . et al J Med Chem 24:1388;1981; Fendersen, B. A. et al J Exp Med 160:1591;1984) for the development of synthetic **vaccines** against tumors (Toyokuni, T. et al Tetrahedron Lett 31:2673;1990). Conjugation of polysaccharides (which are often **T-cell independent**) to protein carriers has been used to convert them into T-cell dependent antigens with enhanced immunogenicity, which have the potential to be **vaccine** candidates (Jennings, H. J. Adv Carb Chem Biochem 41:155;1983).

US PAT NO: 5,653,977 [IMAGE AVAILABLE] L4: 8 of 34

SUMMARY:

BSUM(5)

Although gangliosides would be useful as **vaccines**, they are difficult to produce. Furthermore, some gangliosides are only weakly immunogenic. Those that are immunogenic may not be found on all tumor cells. In humans, the GD2 antigen is weakly immunogenic and generally induces **T cell-independent** humoral immune responses (Tai, T. et al, 1985, Int. J. Cancer 35:607; Portoukalian et al., Int. J. Cancer, 49:893-899 (1991)).

US PAT NO: 5,648,241 [IMAGE AVAILABLE] L4: 9 of 34

DETDESC:

DETD(6)

Differences in immunogenicity have also been observed with the capsular polysaccharides of other bacteria. For example, the **vaccine** against the type C meningococcal capsule is highly active while the group B meningococcal polysaccharide **vaccine** is not immunogenic (Kasper, D. L, et al., J. Infec. Dis. 153:407-415 (1986)). **T-cell independent** functions of the host's immune system are often required for mounting an antibody response to polysaccharide antigens. The lack of a **T-cell independent** response to polysaccharide antigens may be responsible for the low levels of antibody against group B Streptococcus present in mothers. . . B Streptococcus. In addition, children prior to 18 or 24 months of age have a poorly developed immune response to **T-cell independent** antigens.

DETDESC:

DETD(21)

The present invention surmounts the above-discussed deficiencies of prior **vaccines** to group B Streptococcus through the development of a conjugate **vaccine** in which the capsular polysaccharides are covalently linked to a protein backbone. This approach supports the development of a T-cell dependent antibody response to the capsular polysaccharide antigens and circumvents the **T-cell independent** requirements for antibody production (Baker, C. J, et al., Rev. of Infec. Dis. 7:458-467 (1985), Kasper, D. L. et al.,. . .

US PAT NO: 5,587,364 [IMAGE AVAILABLE] L4: 10 of 34

SUMMARY:

BSUM(25)

Literature . . . in host defense systems. This reaction is primarily manifested by increased host surveillance for other antigenie substances. Polysaccharides serve as **adjuvants** (DEAE Dextran, etc.) and immunomodulators. They also can function as unique **T cell-independent** antigens. Both cellular and humoral immunity may be affected, and increased phagocytosis of infectious organisms and tumor cells has been. . .

US PAT NO: 5,476,784 [IMAGE AVAILABLE] L4: 11 of 34

SUMMARY:

BSUM(13)

The . . . derived oligosaccharide (OS) epitope that appears to be widely conserved and expressed amongst clinical isolates of gonococci. Typically, saccharides are **T-cell independent** antigens. When administered alone as immunogens, they generally elicit only a primary antibody response. In addition, oligosaccharides are small (<10. . . saccharide units) (20), and would likely require additional biochemical derivitization to render them immunogenic. The use of such oligosaccharides as **vaccine** candidates, therefore, is limited in several respects.

US PAT NO: 5,474,905 [IMAGE AVAILABLE] L4: 12 of 34

SUMMARY:

BSUM(9)

First, . . . the most common strains of Streptococcus pneumoniae only prevents the subsequent infection by those specific pneumococcal serotypes. Therefore, an individual **vaccinated** by the current **vaccine** would not be protected from a majority of the known serotypes of Streptococcus pneumoniae that cause a variety of diseases. Field studies have shown that the 23-valent capsular **vaccine** provides protection against the **vaccine**-type pneumococcal infection 65% of the time and only protects against all serotypes 0-60% of the time. Second, polysaccharides are not. . . Streptococcus pneumoniae, which are major pathogens in pediatric otitis media and meningitis. Third, the antibody production elicited by polysaccharide is **T-cell independent** and cannot be enhanced by a second immunization. Forth, the immune response to the current **vaccine** in the elderly and children under two years of age is weak and cannot protect them against pneumococcal infection.

SUMMARY:

BSUM(12)

The present invention solves the problems associated with the present antibiotic and **vaccine** therapies for pneumococcal diseases (i.e., diseases caused by Streptococcus pneumoniae). The present invention is directed, inter alia, to isolated hemin/hemoglobin-binding. . . the hemin/hemoglobin-binding proteins described in this invention can serve as antigens for most, if not all, pneumococcal serotypes, are not **T-cell independent** and are prophylactic against pneumococcal infection. A preferred embodiment of this invention is the isolated hemin/hemoglobin-binding protein of Streptococcus pneumoniae. . . art. The present invention provides antibodies to these antigens and compositions containing these antigens. The present invention also provides new **vaccines** and diagnostic methods including kits to both diagnose and treat human pneumococcal infections.

US PAT NO: 5,468,737 [IMAGE AVAILABLE] L4: 13 of 34

SUMMARY:

BSUM(34)

As . . . in host defense systems. This reaction is primarily manifested by increased host surveillance for other antigenic substances. Polysaccharides serve as **adjuvants** (DEAE, Dextran, etc.) and immunomodulators. They also can function as unique **T-cell-independent** antigens. Both cellular and humoral immunity may be affected, and increased phagocytosis of infectious organisms and tumor cells has been. . .

US PAT NO: 5,441,943 [IMAGE AVAILABLE] L4: 14 of 34

SUMMARY:

BSUM(25)

Literature . . . in host defense systems. This reaction is primarily manifested by increased host surveillance for other antigenic substances. Polysacchardies serve as **adjuvants** (DEAE Dextran, etc.) and immunomodulators. They also can function as unique **T cell-independent** antigens. Both cellular and humoral immunity may be affected, and increased phagocytosis of infectious organisms and tumor cells has been. . .

US PAT NO: 5,441,942 [IMAGE AVAILABLE] L4: 15 of 34

DETDESC:

DETD(70)

In summary, T cell-mediated effects of the **adjuvanticity** of guanosine analog derivatives are not ruled out by the observation of T-independence for that **adjuvanticity**, i.e., the existence of a **T cell-independent** phase. Thus, more substantial enhancement can be observed from a composition containing the guanosine analog derivative under conditions of stimulation with T-dependent and T-independent type 2 antigens (T cell dependent situations) than with T-independent type 1 antigens (more completely **T cell-independent**), which suggests the presence of a T cell-dependent component. Moreover, guanosine analog derivatives are thought to act (either directly or. . .

US PAT NO: 5,439,907 [IMAGE AVAILABLE] L4: 16 of 34

DETDESC:

DETD(75)

In summary, T cell-mediated effects of the **adjuvanticity** of substituted guanine derivatives are not ruled out by the observation of T-independence for that **adjuvanticity**, i.e., the existence of a **T cell-independent** phase. Thus, more substantial enhancement can be observed from a composition containing the substituted guanine derivative under conditions of stimulation with T-dependent and T-independent type 2 antigens (T cell dependent situations) than with T-independent type 1 antigens (more completely **T cell-independent**), which suggests the presence of a T cell-dependent component. Moreover, substituted guanine derivatives are thought to act (either directly or. . .

US PAT NO: 5,409,703 [IMAGE AVAILABLE] L4: 17 of 34

SUMMARY:

BSUM(36)

As . . . in host defense systems. This reaction is primarily manifested by increased host surveillance for other antigenic substances. Polysaccharides serve as **adjuvants** (DEAE, Dextran, etc.) and immunomodulators. They also can function as unique **T-cell-independent** antigens. Both cellular and humoral immunity may be affected, and increased phagocytosis of infectious organisms and tumor cells has been. . .

US PAT NO: 5,382,580 [IMAGE AVAILABLE] L4: 18 of 34

DETDESC:

DETD(75)

In summary, T cell-mediated effects of the **adjuvanticity** of substituted guanine derivatives are not ruled out by the observation of T-independence for that **adjuvanticity**, i.e., the existence of a **T cell-independent** phase. Thus, more substantial enhancement can be observed from a composition containing the substituted guanine derivative under conditions of stimulation with T-dependent and T-independent type 2 antigens (T cell dependent situations) than with T-independent type 1 antigens (more completely **T cell-independent**), which suggests the presence of a T cell-dependent component. Moreover, substituted guanine derivatives are thought to act (either directly or. . .

US PAT NO: 5,370,871 [IMAGE AVAILABLE] L4: 19 of 34

ABSTRACT:
The present invention relates to a **vaccine** derived from a bacterial or virus product that initially comprises a mixture of polymers of varying molecular weights. The **vaccine** contains an immunogenically effective polymer comprising **T-cell-independent** antigen as the effective immunizing agent. The **vaccine** is free of low molecular weight immunosuppressive antigen-containing polymer as a result of processing of the bacterial or virus product. . .

DETDESC:

DETD(26)

It . . . flexible linear polymer are immunogenic only if they have a sufficient number of adequately spaced haptens. This finding with a **T cell-independent** antigen might at first seem contradictory to the fact that many protein molecules that are T cell-dependent antigens and which. . . It is well-known that experimentally induced aggregation of protein molecules by physical methods (heat, adsorption to bentonite, emulsification with Freund's **adjuvant**) or by chemical methods (cross-linking with glutaraldehyde or alum) greatly enhances their antigenicity. Nonaggregated protein molecules centrifuged free of aggregates. . . antigenic sites produces an immune response. Therefore, it is possible that the minimum requirements for antigenicity as determined with simple **T cell-independent** polymer may have applicability to immune responses to a large variety of molecules, including T cell-dependent ones. It is in. . .

US PAT NO: 5,317,013 [IMAGE AVAILABLE] L4: 20 of 34

DETDESC:

DETD(55)

T cell-mediated effects of the **adjuvanticity** of 8-MGuo are not ruled out by the observation of T-independence for that **adjuvanticity**, i.e., the existance of a **T cell-independent** facet does not bear upon the existance of a T cell-dependent phase. Thus, more substantial enhancement by compositions containing the. . . doses of T-dependent and T-independent type 2 antigens (T cell dependent situations) than with T-independent type 1 antigens (more completely **T cell-independent**), which suggests the presence of a T cell-dependent component.

DETDESC:

DETD(111)

Thus, the TRF-like effect of 8-MGuo is entirely IL-2 independent. Moreover, the **adjuvant** increase induced by contacting cells with compositions containing 8-MGuo over cultures containing T cells and antigen but without 8-MGuo was also **T cell independent** and IL-2 independent. Therefore, the compositions of this invention acted as substitutes for either intact T cells or soluble T. . .

US PAT NO: 5,308,838 [IMAGE AVAILABLE] L4: 21 of 34

SUMMARY:

BSUM(25)

Literature . . . in host defense systems. This reaction is primarily manifested by increased host surveillance for other antigenic substances. Polysaccharides serve as **adjuvants** (DEAE Dextran, etc.) and immunomodulators. They also can function as unique **T cell-independent** antigens. Both cellular and humoral immunity may be affected, and increased phagocytosis of infectious organisms and tumor cells has been. . .

US PAT NO: 5,166,141 [IMAGE AVAILABLE] L4: 22 of 34

DETDESC:

DETD(66)

T cell-mediated effects of the **adjuvanticity** of guanosine analog derivatives are not ruled out by the observation of T-independence for that **adjuvanticity**; i.e., the existance of a **T cell-independent** facet does not bear upon the existance of a T cell-dependent phase. Thus, more substantial enhancement can be observed from. . . doses of T-dependent and T-independent type 2 antigens (T cell dependent situations) than with T-independent type 1 antigens (more completely **T cell-independent**), which suggests the presence of a T cell-dependent component. Moreover, guanosine analog derivatives are thought to act (either directly or. . .

US PAT NO: 5,147,636 [IMAGE AVAILABLE] L4: 23 of 34

DETDESC:

DETD(55)

T cell-mediated effects of the **adjuvanticity** of 8-MGuo are not ruled out by the observation of T-independence for that **adjuvanticity**, i.e., the existance of a **T cell-independent** facet does not bear upon the existance of a T cell-dependent phase. Thus, more substantial enhancement by compositions containing the. . . doses of T-dependent and T-independent type 2 antigens (T cell dependent situations) than with T-independent type 1 antigens (more completely

T cell-independent), which suggests the presence of a T cell-dependent component.

DETDESC:

DETD(112)

Thus, the TRF-like effect of 8-MGuo is entirely IL-2 independent. Moreover, the **adjuvant** increase induced by contacting cells with compositions containing 8-MGuo over cultures containing T cells and antigen but without 8-MGuo was also **T cell independent** and IL-2 independent. Therefore, the compositions of this invention acted as substitutes for either intact T cells or soluble T. . .

US PAT NO: 5,126,131 [IMAGE AVAILABLE] L4: 24 of 34

DETDESC:

DETD(27)

It . . . flexible linear polymer are immunogenic only if they have a sufficient number of adequately spaced haptens. This finding with a **T cell-independent** antigen might at first seem contradictory to the fact that many protein molecules that are T cell-dependent antigens and which. . . It is well-known that experimentally induced aggregation of protein molecules by physical methods (heat, adsorption to bentonite, emulsification with Freund's **adjuvant**) or by chemical methods (cross-linking with glutaraldehyde or alum) greatly enhances their antigenicity. Nonaggregated protein molecules centrifuged free of aggregates. . . antigenic sites produces an immune response. Therefore, it is possible that the minimum requirements for antigenicity as determined with simple **T cell-independent** polymer may have applicability to immune responses to a large variety of molecules, including T cell-dependent ones. It is in. . .

US PAT NO: 5,118,673 [IMAGE AVAILABLE] L4: 25 of 34

SUMMARY:

BSUM(25)

Literature . . . in host defense systems. This reaction is primarily manifested by increased host surveillance for other antigenic substances. Polysaccharides serve as **adjuvants** (DEAE Dextran, etc.) and immunomodulators. They also can function as unique **T cell-independent** antigens. Both cellular and humoral immunity may be affected, and increased phagocytosis of infectious organisms and tumor cells has been. . .

US PAT NO: 5,106,616 [IMAGE AVAILABLE] L4: 26 of 34

SUMMARY:

BSUM(25)

As . . . in host defense systems. This reaction is primarily manifested by increased host surveillance for other antigenic substances. Polysaccharides serve as **adjuvants** (Freund's, etc.) and immunomodulators. They also function as unique **T cell-independent** antigens. Both cellular and humoral immunity may be affected, and increased phagocytosis of infectious organisms and tumor cells has been. . .

US PAT NO: 5,102,663 [IMAGE AVAILABLE] L4: 27 of 34

SUMMARY:

BSUM(4)

In . . . the serologic response to GM2 and other gangliosides (14-15): pretreatment with low dose cyclophosphamide and immunization with GM2 attached to **adjuvant**-carriers such as BCG or Salmonella minnesota mutant R595. Trials comparing these approaches in early stage melanoma patients demonstrated BCG to be a significantly better **adjuvant** than R595 and patients pretreated with a low dose of cyclophosphamide had significantly higher titers of anti-GM2 antibody than those not receiving this pretreatment (12). IgM antibodies were induced in 72% of patients receiving the BCG-GM2 **vaccine**, and these were capable of lysing human tumor cells in the presence of human complement. IgG antibodies were detected in. . . immunized patients. The pattern of primary and secondary antibody response to immunization was most consistent with GM2 acting as a **T cell independent** antigen.

US PAT NO: 4,948,730 [IMAGE AVAILABLE] L4: 28 of 34

DETDESC:

DETD(55)

T cell-mediated effects of the **adjuvanticity** of 8-MGuo are not ruled out by the observation of T-independence for that **adjuvanticity**, i.e., the existance of a **T cell-independent** facet does not bear upon the existance of a T cell-dependent phase. Thus, more substantial enhancement by compositions containing the. . . doses of T-dependent and T-independent type 2 antigens (T cell dependent situations) than with T-independent type 1 antigens (more completely **T cell-independent**), which suggests the presence of a T cell-dependent component.

DETDESC:

DETD(111)

Thus, the TRF-like effect of 8-MGuo is entirely IL-2 independent. Moreover, the **adjuvant** increase induced by contacting cells with compositions containing 8-MGuo over cultures containing T cells and antigen but without 8-MGuo was also **T cell independent** and IL-2 independent. Therefore, the compositions of this invention acted as substitutes for either intact T cells or soluble T. . .

US PAT NO: 4,900,675 [IMAGE AVAILABLE] L4: 29 of 34

DETDESC:

DETD(85)

T cell-mediated effects of the **adjuvanticity** of isoxanthopterin derivatives are not ruled out by the observation of T-independence for that **adjuvanticity**; i.e., the existance of a **T cell-independent** fact does not bear upon the existance of a T cell-dependent phase. Thus, more substantial enhancement can be observed from. . . doses of T-dependent and T-independent type 2 antigens (T cell dependent situations) than with T-independent type 1 antigens (more completely **T cell-independent**), which suggests the presence of a T cell-dependent component. Moreover, isoxanthopterin derivatives are thought to act (either directly or indirectly). . .

US PAT NO: 4,894,229 [IMAGE AVAILABLE] L4: 30 of 34

SUMMARY:

BSUM(20)

Chedid et al (mol immunol 1980, 17, No 3,357-63 have described synthetic **vaccines** comprising covalent conjugates of muramyl dipeptide derivatives (MDP) and haptens or antigens. MDP is a peptide component of cell walls. . . . extent. Also, for example, if LPS or an LPS derivative is used as a carrier, the conjugate acts as a **T cell independent** immunogen. This limits the carrier to operating via this particular mechanism and limits the response of the immune system.

US PAT NO: 4,849,411 [IMAGE AVAILABLE] L4: 31 of 34

DETDESC:

DETD(56)

T cell-mediated effects of the **adjuvanticity** of 8-MGuo are not ruled out by the observation of T-independence for that **adjuvanticity**, i.e., the existance of a **T cell-independent** facet does not bear upon the existance of a T cell-dependent phase. Thus, more substantial enhancement by compositions containing the. . . doses of T-dependent and T-independent type 2 antigens (T cell dependent situations) than with T-independent type 1 antigens (more completely **T cell-independent**), which suggests the presence of a T cell-dependent component.

DETDESC:

DETD(112)

Thus, the TRF-like effect of 8-MGuo is entirely IL-2 independent. Moreover, the **adjuvant** increase induced by contacting cells with compositions containing 8-MGuo over cultures containing T cells and antigen but without 8-MGuo was also **T cell independent** and IL-2 independent. Therefore, the compositions of this invention acted as substitutes for either intact T cells or soluble T. . .

US PAT NO: 4,762,713 [IMAGE AVAILABLE] L4: 32 of 34

SUMMARY:

BSUM(39)

The . . . a "T cell-dependent" response. Inactive CPs behave much like haptens because they are only weakly antigenic when administered alone as **vaccines**. To the extent they are immunogenic, they do not promote the involvement of helper T cells. Once conjugated to suitable. . . these CPs also produce a "T cell-dependent" response and high antibody titers. Moreover, this response may be "boosted" by subsequent **vaccinations**, unlike the "**T cell-independent**" response that occurs when unconjugated CPs are administered.

US PAT NO: 4,643,992 [IMAGE AVAILABLE] L4: 33 of 34

DETDESC:

DETD(55)

T cell-mediated effects of the **adjuvanticity** of 8-MGuo are not ruled out by the observation of T-independence for that **adjuvanticity**, i.e., the existance of a **T cell-independent** facet does not bear upon the existance of a T cell-dependent phase. Thus, more substantial enhancement by compositions containing the. . . doses of

T-dependent and T-independent type 2 antigens (T cell dependent situations) than with T-independent type 1 antigens (more completely **T cell-independent**), which suggests the presence of a T cell-dependent component.

DETDESC:

DETD(111)

Thus, the TRF-like effect of 8-MGuo is entirely IL-2 independent. Moreover, the **adjuvant** increase induced by contacting cells with compositions containing 8-MGuo over cultures containing T cells and antigen but without 8-MGuo was also **T cell independent** and IL-2 independent. Therefore, the compositions of this invention acted as substitutes for either intact T cells or soluble T. . .

US PAT NO: 4,539,205 [IMAGE AVAILABLE] L4: 34 of 34

DRAWING DESC:

DRWD(119)

Thus, the TRF-like effect of 8-MGuo is entirely IL-2 independent. Moreover, the **adjuvant** increase induced by contacting cells with compositions containing 8-MGuo over cultures containing T cells and antigen but without 8-MGuo was also **T cell independent** and IL-2 independent. Therefore, the compositions of this invention acted as substitutes for either intact T cells or soluble T. . .